Goji (Fruits of *Lycium* spp.): Traditional Uses, Quality Assessment, and Value Chain Analysis

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I meet the long winter of Zurich for the fifth time. The botanical garden likes the cold but lively Swiss winter, by when it is embraced by the odorous witch hazels (*Hamamelis mollis* Oliver), dressed up by the shy snowdrops (*Leucojum* spp.), and kissed by the passionate saffron (*Crocus* spp.). Everything is just as beautiful as the the first sight we met, however, for me, it is the time to leave. To bid farewell to some place where you wrote lots of stories (include but not limited to the academic articles) is never comfortable, and gratitudes are always to the fullest to the nice people there.

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AUTHOR CONTRIBUTIONS TO CHAPTERS

General Introduction

Drafted by Ruyu Yao, revised by Caroline Weckerle and Michael Heinrich.

Chapter 1: The genus *Lycium* as food and medicine: A botanical, ethnobotanical and historical review

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All authors developed the concept for the study; R. Yao conducted the literature survey and drafted the paper. C.S. Weckerle and M. Heinrich supervised the work, and revised the manuscript.

Chapter 2: Quality variation of goji (fruits of *Lycium* spp.) in China: A comparative morphological and metabolomic analysis

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RY, CSW, MH, and YZ developed the concept for the study. RY drafted the paper. CSW and MH supervised the study. Plant materials were collected by RY and YC; morphological traits were measured by XZ and RY; HPTLC was supervised by ER and analyzed by RY; ^{1}H NMR was analyzed by RY at MH's lab and under his supervision; contents of sugar was measured by RY and YC; antioxidant activity was measured by YZ and YC. Data were analyzed by RY, YZ, ER, XZ, and YC. All authors revised the paper.

Chapter 3: Quality control of goji (fruits of *Lycium* spp.): A value chain analysis perspective

Ruyu Yao, Michael Heinrich, Zigui Wang, Caroline S. Weckerle

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RY, CSW, and MH developed the concept for the study. RY and ZW drafted the paper. CSW and MH supervised the study. Fieldworks were conducted by RY with the critical help of ZW; plant materials were collected by RY and ZW; pesticides residue, and sulphur residue were measured by RY; ZW contributed critical financial data and behaviour information, and value chain analysis was carried out by RY and ZW. Data were analysed by RY and ZW. All authors revised the paper.

ZUSAMMENFASSUNG

Traditionell genutzte Pflanzen und Pflanzenprodukte finden vermehrt Eingang in den globalen Markt. Dies wirft Fragen auf im Bereich der Wirksamkeit und Toxikologie von Produkten, zu Qualitätsstandarts und zur Versorgung des Marktes mit den notwendigen Mengen an Pflanzenmaterial. Die vorliegende Dissertation widmet sich den Goji Beeren (*Lycium* spp.), die seit Jahrtausenden medizinisch und kulinarisch genutzt werden und heute global als gesundheitsfördernder Nahrungsmittelzusatz gehandelt werden.

Das erste Kapitel widmet sich der Nutzungsgeschichte von *Lycium* weltweit, und mit einem Fokus auf Ostasien. Von weltweit insgesamt 97 Arten werden ca. 35 medizinisch und als Nahrung genutzt. *Lycium barbarum* L. und *L. chinense* Mill., beide aus Ostasien stammend, wurden globalisiert und *L. barbarum* wird in China im grossen Stil angebaut. Die Verwendung der beiden Arten kann in China mittels historischer Textquellen über die letzten 2000 Jahre zurückverfolgt werden. Aktuelle medizinische Verwendungen mit historischem Hintergrund umfassen die Augengesundheit und die Nutzung als allgemeines Stärkungsmittel. Diese Anwendungen werden durch pharmakologische Studien gestützt. Aufgrund der historischen Dokumente ist eine vielfältigere Anwendung von Goji Produkten sowie die Verwendung zusätzlicher Arten denkbar.

Im zweiten Kapitel werden Goji Proben aus klimatisch unterschiedlichen Anbauregionen Chinas aufgrund ihrer Inhaltsstoffe und Morphologie der Früchte miteinander verglichen. Ursprünglich wurde Goji im Osten des Landes in der Provinz Hebei angebaut, von wo aus sich der Anbau nach Westen in trockenere Gebiete hinein ausgedehnt hat. Heute gilt Ningxia in China als *daodi* Gebiet, d.h. als Region aus der die besten Goji Beeren kommen. Unsere Analysen stützen diese Aussage nicht. Metabolomische Unterschiede finden sich zwischen den Arten *L. barbarum* und *L. chinense*, nicht aber zwischen den Anbauregionen. *L. chinense* hat eine höhere antioxidative Aktivität als *L. barbarum*, und *L. barbarum* aus ariden Regionen zeigt den höchsten Zuckergehalt. Der metabolomische Ansatz kombiniert mit morphologischen Parametern ermöglicht es, verschiedene Typen von Goji zu charakterisieren, die sich für unterschiedliche medizinische und kulinarische Anwendungen anbieten.

Im dritten Kapitel werden Wertschöpfungsketten von Goji analysiert, die sich bezüglich Produktequalität, Rückverfolgbarkeit und Verunreinigungen von Produkten unterscheiden. Dabei werden zehn verschiedene Formen von Ketten charakterisiert und diskutiert, und die

Wertschöpfung der verschiedenen Beteiligten vergleichend angeschaut. Obschon die Bauern einen grossen Beitrag zur Bearbeitung der Beeren leisten, sind sie im Allgemeinen nur marginal an der Wertschöpfung beteiligt. Es zeigt sich, dass die Wertschöpfung direkt mit der Produktequalität zusammenhängt.

Horizontale Kooperation (z.B. Bauern-Kooperativen) und vertikale Integration zwischen Bauern und Verkäufern zeigen eine positive Auswirkung sowohl auf die Qualität der Produkte als auch auf die Wertschöpfung der Bauern. Wir erwarten, dass vollständig integrierte, vertikale Wertschöpfungsketten in Zukunft weite Verbreitung finden werden.

SYNOPSIS

The popularity of plant-derived high value products as functional foods makes them an interesting research topic in the fields of ethnobotany, phytochemistry, food sciences and pharmacology. For a comprehensive understanding and meaningful use it is important to secure good product quality and to understand the phytochemistry and pharmacology of plant products, but also to relate current with traditional uses. Using an interdisciplinary approach this thesis investigates an Asian traditional herbal food and medicine known as goji (fruits of *Lycium* spp.). Goji has been recently advertised at a global level as "super food". In this work culinary and medicinal uses of *Lycium* spp. in different cultures around the world have been reviewed and the use history in China over the last 2000 years has been analysed and correlated with general pharmacological activities; subsequently, a metabolomic and morphological comparative approach was used to analyze cultivated goji from different climatic regions. Finally, based on a detailed understanding of product quality and stakeholders' behaviour, goji value chains were compared and a quality control strategy from a value chain perspective was developed.

Chapter 1 comprises a systematic ethnobotanical investigation and description of the food and medicinal uses of *Lycium* L. over space and time. Relying on botanical, ethnobotanical and historical sources, it is found that 35 of totally 97 *Lycium* species have been used traditionally. Species and their usages differ among cultures; and, only *L. barbarum* L. and *L. chinense* Mill. from East Asia have been transformed into globally traded commodities. According to recent and historical Chinese herbals, their use can be traced back over the last two millennia. Recent applications with a historical record include improving eyesight as well as anti-aging and anti-fatigue. The pharmacological foundation of traditional and recent uses is mainly based on the following constituents / groups of compounds of the fruits: polysaccharides, zeaxanthin dipalmitate, vitamins, and betaine. Several national Pharmacopoeias adopt goji as a medicine, but quality criteria as well as the species they refer to differ among countries. We suggest that new food and medicinal products of lesser known *Lycium* spp. could be developed based on their traditional usages, and new uses of *L. barbarum* and *L. chinense* might be explored according to the historical records.

Chapter 2 investigates the quality of commercial goji from different climatic regions of China. Our results do not justify superiority of a specific production area over other areas, despite the fact that Ningxia is accepted as *daodi* region which means that it is acclaimed to produce the best goji. Many other regions are named as “home of goji”, indicating that they produce outstanding goji. Historically, goji was first cultivated in Hebei (monsoon climate) and from there transferred westwards into drier habitats. Goji from the monsoon, plateau and arid regions differ according to fruit morphology, but are not distinguishable from fruits of semi-arid cultivation regions. Metabolomic profiling separates the two species *L. barbarum* and *L. chinense*, but not the cultivation regions. *L. chinense* and samples from the semi-arid regions have significantly ($p < 0.01$) lower sugar contents and *L. chinense* shows the highest antioxidant activity. The metabolomic approach used combined with morphological analysis and bioactivity evaluation allows for capturing different goji quality clusters, and allows detecting different species. Therefore, we suggest using goji from different regions for different purposes, based on the specific morphological and chemical traits.

Chapter 3 focuses on value chains of goji and quality control. Value chains of goji are mapped, while production behaviours and financial performances of stakeholders along the value chains are analysed. The traceability, reputation of products, and the probability of chemical contaminations of goji differ amongst value chains. Stakeholders’ revenue, behaviours, and quality of goji are correlated; horizontal collaborations and vertical integrations in value chains are beneficial to both quality and financial performance, while well-developed vertical integrated value chains are expected to become more important in the future.

GENERAL INTRODUCTION

Ethnobotany: investigation of traditional plant knowledge

We share our planet with over 374’000 plant species (Christenhusz and Byng, 2016). Plants are indispensable for humans: Besides their basic function of oxygen production, they produce food (directly or indirectly), offer building material for houses, yield fiber for clothes, and can be used as ornamentals, fuel, dye, and medicine. It is estimated that between 50’000 and 80’000 flowering plant species are used for medicinal purposes worldwide (Chen et al., 2016). In China alone, 11’146 plant species have been documented for their medicinal use, which is around one third of the total flora (Chen et al., 2010). Plant usage is shaped by culture and accessibility (e.g., Heinrich et al., 1998; Hsu and Harris, 2010; Weckerle et al., 2006). As a result, people of different cultural backgrounds have been accumulating a wealth of knowledge on useful plants from their environments.

Ethnobotany studies traditional plant knowledge and supports both, the understanding of cultural traditions and the conservation of biocultural diversity. It investigates the broad field of human plant interactions, and stretches into healthcare, drug discovery, or ritual culture (Flitsch, 1999; Heinrich, 2000; Heinrich et al., 2006; Hsu and Harris, 2010; Qureshi et al., 2016; Staub et al., 2011a; Staub et al., 2011b; Weckerle et al., 2011; Yeung et al., 2018). For example, the discovery of artemisinin, an important anti-malaria compound, was inspired by the traditional use of *Artemisia annua* L. in Chinese Medicine (Tu, 2011; Tu, 2016). However, if traditional knowledge is misinterpreted it can become problematic: For example, the misuse of *Aristolochia*-related species, either due to adulteration or confusion of names, has caused renal failure in patients (Wu, 2007). Therefore, in-depth knowledge about traditional uses of plants is important for correct and safe use.

Edible herbal medicine or functional food for good health

Indigenous people often do not separate stringently between food and medicinal plants. Food as medicine and medicine as food is an integral part of all traditional medicinal systems for prevention of disease and promotion of health (Etkin and Ross, 1982). To stay healthy, wild collected food plants are traditionally used for soups, as boiled vegetables, in pies, salads, teas, jams, or as raw snack (Abbet et al., 2014; Guarrera and Savo, 2016; Leonti et al., 2006; Sansanelli and Tassoni, 2014). Plants also have a long history as medicines and still play an important role in biomedicine as well as alternative and complementary medicinal systems and traditional rural contexts (Chen et al., 2016; Dal Cero et al., 2014; Hamilton, 2004).

The usage of plants as medicine and food is continuous, and plants used for both medicine and food may be described as “edible herbal medicines” (Dal Cero, 2016; Etkin and Ross, 1982; Jennings et al., 2015; Kimondo et al., 2015; Quave and Pieroni, 2015; Rivera et al., 2005; Towns and Van Andel, 2016). Edible herbal medicines have nutritional properties like common foods, but at the same time can be used as therapeutics. Today, they are typically known as functional food or nutraceuticals and are part of the global market (Guarrera and Savo, 2016; Valussi and Scirè, 2012). In China, the State Food and Drug Administration announced that 88 herbal medicines registered in the Chinese pharmacopoeia are also permitted to be used as food; however, the integration of medicinal plants into daily diet is very common in China and many more species are used for this purpose; Medical diet as therapy or for prevention is an integral part of Chinese Medicine (Tan et al., 2017; Xu, 2001). Health benefits of functional foods are related to bioactive compounds. For example, specific polysaccharides are known for their immunomodulatory effect, flavonoids exhibit antioxidative activity, caffeine stimulates the central nervous system, and phytosterols support heart health (Guarrera and Savo, 2016; Hilton, 2017; Xie et al., 2016). Since health is of major concern in our time, functional foods are increasingly in demand. The world market is estimated to 150 billion USD per year, with an annual growth of over 10% (Hilton, 2017).

Quality control: assurance of safety and effectiveness

Increasing trade and consumption of plant products comes along with a number of challenges, such as resource shortage or depletion, and quality variation of plant material (Booker et al., 2016b; Cassiday, 2017). The over-collection of wild plant resources can threaten species and cause ecological damage (Booker et al., 2016b; Wang et al., 2017; Winkler, 2011). It is estimated that worldwide up to 15’000 medicinal species are threatened and 20% of them are at the edge of extinction (Chen et al., 2016). Shortage may lead to substitution, adulteration or fake products (Booker et al., 2016b; Luo et al., 2018; Shi et al., 2017). Cultivation can be a valuable option for medicinal plant production; but, the use of pesticides and herbicides may negatively influence product quality (Chen et al., 2016; Hoban et al., 2017; Li et al., 2017; Wang et al., 2017; Yao et al., 2012). Therefore, quality of herbal medicine is of major concern, and quality control is critical for safe and efficacious use.

Comprehensive quality inspection includes 1) reliable identification of plant material, 2) assurance of relevant bioactive compounds in the plant material, and 3) restriction and detection of harmful constituents (contaminants and impurities as well as endogenous toxic compounds) (**Figure 1**).

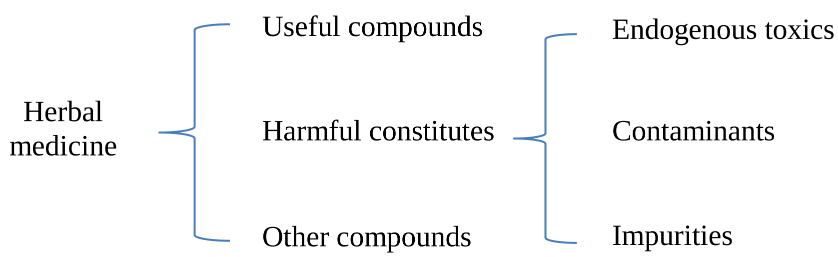

Figure 1 The chemical constitution of a herbal medicine

Species identification and exclusion of adulterants is the primary step of quality control. Beside morphological and anatomical methods, molecular identification, such as DNA barcoding, is frequently used or chemical methods are applied such as HPTLC fingerprinting (Booker et al., 2014; Chen et al., 2010; Raclariu et al., 2017; Xin et al., 2013). Useful bioactive compounds and their amount are detected by chromatographic approaches (Liang et al., 2004; Wagner et al., 2011). However, the relevant constituents for plant activity are not always known and the medicinal effect may be due to a number of compounds influencing each other. This is especially the case for Chinese Medicine where plant mixtures are preferentially administered (Donno et al., 2016). Harmful constituents need to be controlled strictly. Impurities such as dust, fungal or bacterial infections due to moisture are usually caused by improper processing conditions. Contaminants such as pesticide residues, heavy metals, and microbial toxins are frequently found in plant products; detection costs are relatively high and often not affordable for small producers. Harmful endogenous compounds such as aristolochic acid only occur in specific plant groups and need to be tested specifically (Ng et al., 2017). To ensure good quality it needs not only testing and control of plant products, but also regulations for production and processing (Booker and Heinrich, 2016).

Value chain: stakeholders and products

A botanical product always passes through numerous stages of production, such as cultivation, processing, and distribution, before it reaches the final consumers (Székács et al., 2018). Therefore, the quality of plant products is impacted by many external factors, until they enter the global market. A number of regulatory frameworks are applied to control the procedures, such as the Hazard Analysis Critical Control Point (HACCP) of the FDA (USA), Good Agricultural Practice (GAP), and those of EMA/EFSA (EU); however, these regulations have their limitations and are not sufficient to guarantee good quality of plant products (Huang et al., 2017; Sperber, 2005; Will and Guenther, 2007; Yao et al., 2012).

A value chain comprises all movements from the raw material to the final product across all parties involved, and can represent exhaustive flows of material, funds, and information (Datta, 2017; Lovis, 2008; Mentzer et al., 2001; Opara, 2003; Regattieri et al., 2007). Value chains affect both the quality of herbal products and the welfare of the stakeholders (Booker et al., 2012; Booker et al., 2016a; Heinrich, 2015). As a concept value chains connect the products with the stakeholders; and, with an interdisciplinary approach, they can be used as a tool to improve overall quality. This may include traceability of products, behaviour of stakeholders as well as revenue of stakeholders.

Goji (fruits of *Lycium* spp.): from local to global

In Asian countries goji, or wolfberry, has been used for at least 2000 years as a traditional food and medicine. Today, the global market advertises it as "super food". The present thesis studies goji as a case study of a plant that was locally important for centuries before it became a global product. The thesis sheds light at its uses and trade over time from the above introduced perspectives:

Traditional and recent knowledge of *Lycium* species is analysed from a botanical, ethnobotanical and historical perspective. Phytochemical and morphological approaches are used to characterize the quality of cultivated goji from different climatic regions in China, and, the different value chains involved in goji production were documented and are analysed for their potential to increase goji quality as well as fair sharing of revenues among stakeholders.

There is an old saying in Chinese Medicine: “good medicinal plant material results in good drugs” (药材好，药才好; yào cái hǎo, yào cái hǎo). Hopefully, this study contributes to our deepened scientific understanding of this very process.

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CHAPTER 1

The genus *Lycium* as food and medicine: A botanical, ethnobotanical and historical review

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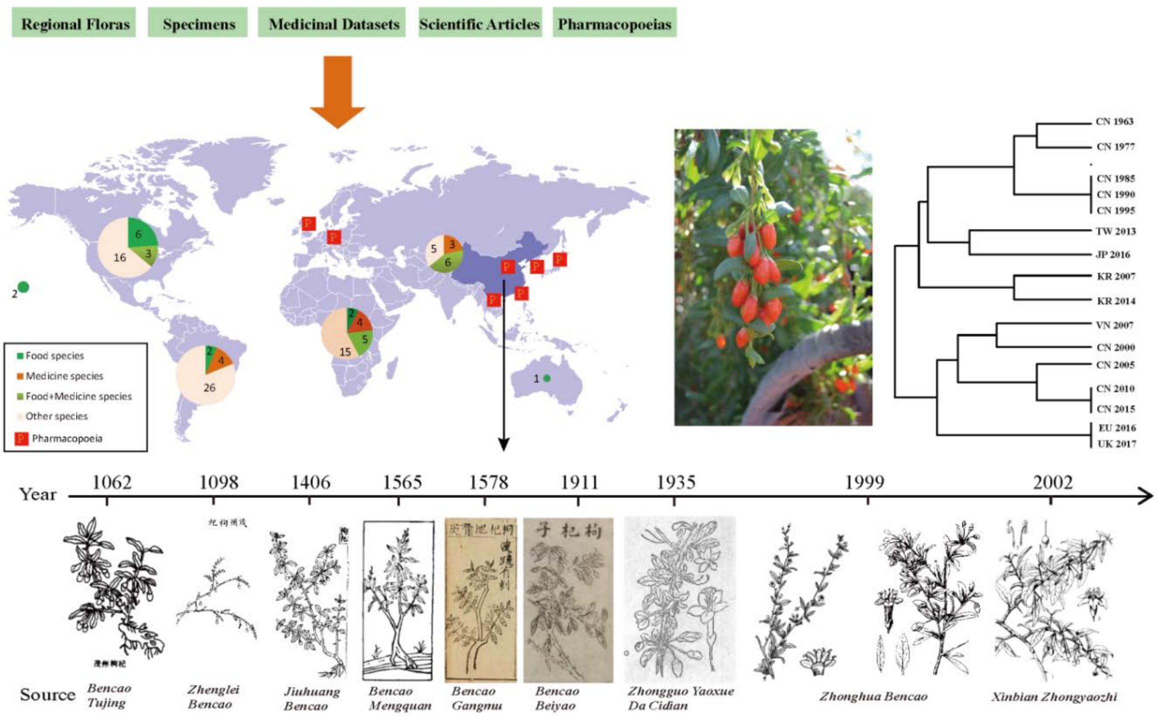

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The genus *Lycium* as food and medicine: A botanical, ethnobotanical and historical review

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ABSTRACT

Ethnopharmacological relevance: *Lycium* is widely distributed in the arid to semi-arid environments of North and South America, Africa, and Eurasia. In recent years, *Lycium barbarum* and *L. chinense* have been advertised as "superfood" with healthy properties. Despite of its popularity, there is a lack of an integrated and critical appraisal of the existing evidence for the use of *Lycium*.
Aim of the study: There is a need to understand: 1) Which species were used and how the uses of *Lycium* developed spatially and over time, 2) how uses differ among regions with different culture backgrounds, and 3) how traditional and current therapeutic and preventive health claims correlate with pharmacological findings.
Methods: Information was retrieved from floras, taxonomic, botanical, and ethnobotanical databases, research articles, recent editions of historical Chinese herbals over the last 2000 years, and pharmacopoeias.
Results: Of totally 97 species, 35 have recorded uses as food and/or medicine worldwide. Usually the fruits are used. While 85% of the *Lycium* species occur in the Americas and Africa, 26% of them are used, but 9 out of 14 species in Eurasia. In China, seven species and two varieties of the genus *Lycium* occur, of which four species have been used by different ethnic groups. Only *L. barbarum* and *L. chinense* have been transformed into globally traded commodities. In China, based on the name "枸杞", their use can be traced back over the last two mil-lennia. *Lycium* fruits for anti-aging, improving eyesight and nourishment were documented already in 500 C.E.(*Mingyi Bielu*). Recent findings explain the pharmacological foundations of the traditional uses. Especially polysaccharides, zeaxanthin dipalmitate, vitamins, betaine, and mixed extracts were reported to be responsible for anti-aging, improving eyesight, and anti-fatigue effects.
Conclusions: The integration of historical, ethnobotanical, botanical, phytochemical and pharmacological data has enabled a detailed understanding of *Lycium* and its wider potential. It highlights that the focus so far has only been on two species and that the genus can potentially yield a wide range of other products with different properties.

1. Introduction

Plant-based products are important sources of both food and medicine. Whether a plant is used as food or medicine depends on a wide range of factors, but is not necessarily intrinsic to its pharmacological or nutritional properties (Leonti, 2011; Jennings et al., 2015). In the last decades the variety of consumed crops has increased globally, especially of local agricultural varieties and species collected from the wild. These are becoming more important for human nutrition and for medicinal uses (Heywood, 2011). This increase is often based on traditional knowledge, which is defined as knowledge innovations and practices of indigenous and local communities embodying traditional lifestyles relevant for the conservation and sustainable use of biological diversity (Xue, 2011). Traditional knowledge on plants can be used as a starting point to develop new medicines, e.g., the discovery of artemisinin (Tu, 2015), while it should be protected subject to the Nagoya Protocol (Ngo et al., 2013; Buch and Hamilton, 2011). Therefore, traditional knowledge on plants continues to play an important role in human lives for both food and medical purposes.

The fruit, leaf, root bark, and young shoot of many species of the genus *Lycium* L. have long been used as local foods and/or medicines. Recently, *Lycium* fruits, known as goji or wolfberry, have become increasingly popular in the western world because of their nutritional properties (Qian et al., 2017; Amagase, 2010; Potterat, 2010; Amagase and Farnsworth, 2011); they are even advertised as "superfood" in Europe and North America (Wolfe, 2010; Chang and So, 2015).

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Table 1
Data sources used.

Themes	Data sources	Key words
Taxonomy & Systematics	The Plant List (2013), http://www.theplantlist.org/; GBIF (Global Biodiversity Information Facility), 2017, https://demo.gbif.org/; IPNI (The International Plant Names Index), 2015, http://www.ipni.org/; LycieaeWeb (2017), http://jsmiller.people.amherst.edu/LycieaeWeb/Project_Lycieae.html; African Plant Database (version 3.4.0), 2017. http://www.ville-ge.ch/musinfo/bd/cjb/africa/; EuroPlusMed PlantBase (2011), http://ww2.bgbm.org/; eFloras (2017). http://www.efloras.org; Flora of China (Vol. 17), 1994. http://foc.eflora.cn/; Flora of China (Vol. 67), 1994; Flora of Victoria, 2015, https://vicflora.rbg.vic.gov.au/; Neotropical Flora (2017), http://hasbrouck.asu.edu/neotrop/plantae/index.php; Flora of Israel (2017), http://flora.org.il/plants/; Flora of Pakistan, 1980; Flora of the great plains, 1986; Flora of North America (2009), http://luirig.altervista.org/flora/taxa/north-america.php; NPGS (National Plant Germplasm System), 2016. https://npgsweb.ars-grin.gov/; Flora of Argentina (1992). http://www.floraargentina.edu.ar/; and scientific articles of Google scholar, science direct, web of science, NCBI (National Center for Biotechnology Information), and NEBIS (Network of Libraries and Information Centers in Switzerland).	*Lycium*, and the specific species names.
Traditional uses globally	Dr. Duke's Phytochemical and Ethnobotanical Databases, 1992–2016, http://phytochem.nal.usda.gov/; NPGS (National Plant Germplasm System), 2016. https://npgsweb.ars-grin.gov/; FEIS (Fire Effects Information System), 2016, http://www.feis-crs.org/feis/; NAEB (Native American Ethnobotany Database), 2003. http://naeb.brit.org/; PFAF (Plants for a Future), 2016, http://www.pfaf.org/; ETHMEDmmm (The Data Base of Ethno-medicines in the world), 2016, http://ethmed.u-toyama.ac.jp; Medicinal Plant Names Services (2017) (http://mpns.kew.org); and scientific articles of Google scholar, science direct, web of science, NCBI (National Center for Biotechnology Information), and NEBIS (Network of Libraries and Information Centers in Switzerland).	*Lycium*, the specific species names, Traditional use, food, medicine, ethnobotanical survey.
Use history in Chinese medicine	Chinese herbals and agronomy monographs (from ca. C.E. 100–2006; see S1); regional books of ethnobotany and herbal medicine in China. (Search with" nationality + 医药" in google book (https://books.google.com/).	"杞","地骨皮"
Pharmacopoeias	Chinese Pharmacopoeia (2015, vol. 1), European Pharmacopoeia (9.0), Japanese Pharmacopoeia (16th), Korean Pharmacopoeia (9th), Taiwan TCM Pharmacopoeia (2013), Vietnam Pharmacopoeia (4th), Ayurveda API (Vol. 6); all editions of Chinese Pharmacopoeia (1953–2015) British Pharmacopoeia Commision (2017).	*Lycium*

Phytochemical studies indicate that the richness in numerous constitutions of different classes, such as polysaccharides, carotenoids, flavonoids, alkaloids, amides, terpenoids, and so on, endows *Lycium* species with a variety of biological activities (Qian et al., 2017; Yao et al., 2011). Also, pharmacopoeias adopted the most popular species, *L. barbarum* and/or *L. chinense*, as herbal medicines (Wagner et al., 2011).

Thus, species of the genus *Lycium* serve as widely used source of food and medicine. Despite of its popularity, there is a lack of an integrated and critical appraisal of the existing evidence for the use of *Lycium*. From a botanical and ethnopharmacological perspective, there is a need to understand: 1) Which species were used and how the uses of *Lycium* developed spatially and over time, 2) how uses differ among regions with different culture backgrounds, and 3) how traditional and current therapeutic and preventive health claims correlate with pharmacological findings.

To answer these questions we started with a botanical overview of the genus and its accepted species, and did a comprehensive study and analysis of a large body of literature and databases.

2. Methods

Overall, information was obtained from floras, taxonomic, botanical, and ethnobotanical databases, research articles, recent editions of historical Chinese herbals, and pharmacopoeias. All sources used to extract information as well as the applied keywords are given in Table 1.

For species names and synonyms we relied on The Plant List (2013) and local floras. Distribution data and biogeographic information were obtained from IPNI (2015), GBIF (2017), LycieaeWeb (2017) and research articles. Morphological characters were extracted from the regional floras and type specimens in the Chinese National Herbarium (PE) were consulted for verification.

To gather information about the use of *Lycium* species at a global level, the following strategy was used: 1) "*Lycium*" was used as key word to search within the ethnobotanical databases (Table 1). 2) In google scholar, "*Lycium*" and "traditional" or "ethnobotany" or "medicine" or "food" or "herb" were searched. 3) The validated species names were searched within the ethnobotanical databases and google scholar. And 4) the words "ethnobotanical survey" were searched, then "*Lycium*" was searched in the texts. 5) "*Lycium*" was also searched in regional ethnobotanical and herbal medicine monographs. Results were integrated with species data.

For the history of *Lycium's* use we focused on China, both because a continuous documentation over the last two millennia is available, and the current boom of goji use originated in China. We relied on modern translations of classical Chinese herbals. At least one herbal per dynasty was included. If several contemporary herbals existed, the most comprehensive one and herbals adding new information were used. In total, 32 herbals from ca. C.E. 100–2006 were considered.

In order to find scientific evidence for traditional uses, we did a literature search on the phytochemistry and pharmacology of *Lycium* species. The main bioactivities and the related compounds or extracts were listed in one table.

To compare *Lycium* records in pharmacopoeias of different regions, "*Lycium*" was searched in the pharmacopoeias listed in the Index of the World Pharmacopoeias and Pharmacopoeial Authorities (document QAS/11.453/ Rev.6) published by WHO in 2016. *Lycium* was only found in the pharmacopoeias of seven Asian countries and regions.

In order to study the change of the records over time, all editions (from 1953 to 2015) of the Chinese pharmacopoeia were consulted.

Additionally, all the parameters for *Lycium* fruit and *Lycium* root included in the pharmacopoeias were extracted and analyzed with a cluster analysis to understand the relationships among pharmacopoeias. R and the package "ape" was employed (R Core Team, 2017; Paradis et al., 2004) for cluster analysis.

3. Results

3.1. Botany

The genus *Lycium* (Solanaceae) widely grows in arid to semi-arid environments of the temperate zones (Fukuda, 2001; Miller et al., 2011;

Table 2
The distribution of *Lycium* species and their uses as food and medicine.

Species name	Distribution	Food use	Medicine use	References[a] for plant uses
L. acutifolium E. Mey. ex Dunal	South Africa, Madagascar, Lesotho	Starch of root recommended as famine food for extending bread flour; bark as condiment.	Pounded bark to keep a person in good health	USDA (1992–2016); Dhar et al. (2011); Watt and Warmelo (1930); Lev and Amar (2006); MPNS, 2017
L. afrum L.	South Africa, France, Tunisia, Sweden, Germany, Netherlands, medieval Cairo	Fruit: food	Leaves, fruits, roots for eye diseases, cough	USDA, 1992–2016; PFAF (2016); Middleditch (2012); Lev and Amar (2006); MPNS, 2017
L. ameghinoi Speg.	Argentina	NM (not mentioned)	NM	–
L. americanum Jacq.	Bahamas; Cuba; Haiti; Dominican Republic; Islas de Barlovento; Venezuela; Colombia; Costa Rica; Ecuador; Peru; Bolivia; Paraguay; Argentina	fruit as food	NM	Arenas and Scarpa (2007)
L. amoenum Dammer	South Africa, Namibia	NM	NM	–
L. anatolicum A.Baytop & R.R.Mill	Turkey, Armenia	NM	NM	–
L. andersonii A. Gray	US, Mexico	Fruit as food	NM	NAEB (2003); PFAF (2016); Saunders (1920); Crosswhite (1981); Hodgson (2001); Newton (2013)
L. andersonii var. *deserticola* (C.L. Hitchc.) Jeps.	US, Mexico	NM	NM	–
L. arenicolum Miers	South Africa, Lesotho, Botswana, United States	NM	NM	–
L. athium Bernardello	Argentina	NM	NM	–
L. australe F.Muell.	Australia	Fruit as food	NM	PFAF (2016); Jeanes (1999); Clarke (1998)
L. barbarum L.	Widely distributed in Asia, Europe, North America, and Austria; also appears in Africa and South America	Fruit, shoot, leaf as food	Fruit, root, leaf, calyx, bark, and whole plant as medicines for a variety of diseases	USDA, 1992–2016; PFAF (2016); Lim (2012); Liu et al. (2004); Li et al. (2001); Ali (1964); ETHMEDmm, 2016; Koleva et al. (2015); Duke (2002); Deeb et al. (2013); MPNS, 2017; Quattrocchi (2012)
L. berberioides Correll	US	NM	NM	–
L. berlandieri Dunal	US, Mexico, Germany	Fruit as food	Plant as medicine	FEIS (2016); PFAF (2016); Kearney et al. (1960); Powell, 1988; Newton (2013)
L. berlandieri var. *parviflorum* (A. Gray) A. Terracc.	US, Mexico	Fruit as food	Plant as medicine	Hodgson (2001)
L. bosciifolium Schinz	Namibia, South Africa, Botswana, Angola, Zimbabwe	Leaf as food	NM	Ndithia and Perrin, 2006
L. brevipes Benth.	US, Mexico	NM	NM	–
L. californicum A. Gray	US, Mexico, Jamaica	NM	NM	–
L. carinatum S. Watson	Mexico, Jamaica	NM	NM	–
L. carolinianum Walter	US, Mexico, Cuba, Easter Island, West Indies	fruit as food	NM	PFAF (2016)
L. carolinianum var. *quadrifidum* (Moc. & Sessé ex Dunal) C.L. Hitchc.		NM	NM	–
L. cestroides Schltdl.	Argentina, Bolivia, Uruguay, Brazil, Australia, Germany, UK	NM	Analgesic	Rondina et al. (2008); MPNS, 2017
L. chanar Phil.	Argentina, Bolivia, Chile	NM	NM	–
L. chilense Bertero	Argentina, Chile, Paraguay, Bolivia, UK, Brazil, Switzerland, Ecuador, France	NM	Fruit as medicine	NPGS (2016); USDA, 1992–2016
L. chinense Mill.	Widely distributed in Asia, Europe, North America, and Austria	Fruit, leaf and young shoot as food; seed for coffee; leaf as tea	Fruit, root, leaf, bark, and whole plant as medicines	NPGS (2016); PFAF (2016); USDA, 1992–2016; Lim (2012); ETHMEDmm, 2016; MPNS,2017; Duke (2002); Quattrocchi (2012)
L. chinense var. *potaninii* (Pojark.) A.M.Lu	China	NM	Root bark as medicine	Li et al. (2001)
L. ciliatum Schltdl.	Argentina, Brazil, Bolivia	NM	Leaf as medicine for digestive and stomach inflammations	Trillo et al. (2010); Toledo et al. (2014)
L. cinereum Thunb.	South Africa, Botswana, Namibia, Lesotho	Fruit as food	Treat headache and rheumatism; root: anodyne, kidney disease, perfume	Iwu (2014); Dhar et al. (2011); Van Damme (1998); MPNS, 2017
L. cooperi A. Gray	Mexico, US	NM	NM	–
L. cuneatum Dammer	Argentina, Paraguay, Bolivia	NM	NM	–
L. cyathiformum C.L. Hitchc.	Bolivia, Argentina	NM	NM	–

(*continued on next page*)

Table 2 (*continued*)

Species name	Distribution	Food use	Medicine use	References[a] for plant uses
L. cylindricum Kuang & A. M. Lu	China	NM	NM	–
L. dasystemum Pojark.	China, Iran	Fruit as food	Fruit as medicine	Ali (1980); Azadi et al. (2007); Li et al. (2001);
L. decumbens Welw. ex Hiern	South Africa, Namibia, Angola	NM	NM	–
L. densifolium Wiggins	Mexico	NM	NM	
L. depressum Stocks	Iran, Russia, Israel, Turkmenistan, Iraq, Palestinian Territory, Afghanistan, Turkey, Pakistan, Jordan	NM	Leaf and fruit for kidney problems	Tabaraki et al. (2013); Ghasemi et al. (2013)
L. deserti Phil.	Chile	NM	NM	–
L. dispermum Wiggins	Mexico	NM	NM	–
L. distichum Meyen	Peru, Bolivia, Chile	NM	NM	–
L. divaricatum Rusby	Peru, Bolivia	NM	NM	–
L. edgeworthii Miers	India, Pakistan, Iran	NM	NM	–
L. eenii S. Moore	Namibia	NM	NM	–
L. elongatum Miers	Argentina	NM	Leaf for digestive	Toledo et al., 2014; Trillo et al., 2010.
L. europaeum L.	Spain, France, Israel, Palestinian Territory, Algeria, Portugal, India, Tunisia, Egypt	Fruit and young shoot as food	Fruit, leaf, bark, and whole plant are used for a variety of treatments	PFAF (2016); Fratkin (1996); Dafni and Yaniv (1994); Said et al. (2002); El Hamrouni, 2001; Boullard (2001); Pieroni et al. (2002); Al-Quran (2007); El-Mokasabi (2014); Turker et al. (2012); Leporatti and Ghedira (2009); Licata et al. (2016); MPNS, 2017
L. exsertum A. Gray	US, Mexico	Fruit as food	NM	NAEB (2003); Hodgson (2001); Newton (2013); Nabhan et al. (1982)
L. ferocissimum Miers	Australia, South Africa, New Zealand, Morocco, Namibia, US, Lesotho, Spain, Norfolk Island, Tunisia	Fruit as food	Plant for detoxication of narcotic poisoning	Watt and Breyer-Brandwijk (1962); Arnold et al. (2002); MPNS, 2017
L. fremontii A. Gray	US, Mexico	Fruit as food	NM	NAEB (2003); PFAF (2016); Watt and Breyer-Brandwijk (1962); MPNS, 2017
L. fuscum Miers	Argentina	NM	NM	–
L. gariepense A.M.Venter	South Africa, Namibia	NM	NM	–
L. gilliesianum Miers	Argentina, Chile	NM	NM	–
L. glomeratum Sendtn.	Argentina, Paraguay, Bolivia, Brazil, China	NM	NM	–
L. *grandicalyx* Joubert & Venter	South Africa, Namibia	NM	NM	–
L. hantamense A.M.Venter	South Africa	NM	NM	–
L. hassei Greene	US	NM	NM	–
L. hirsutum Dunal	South Africa, Namibia, Botswana	NM	NM	–
L. horridum Thunb.	South Africa, Namibia, Madagascar, Botswana, Lesotho, Angola, Iran, Mauritius, Turkey	NM	NM	–
L. humile Phil.	Chile, Argentina	NM	NM	–
L. infaustum Miers	Argentina, Colombia, Bolivia, Ecuador, Dominican, Turks And Caicos Islands, Jamaica, Peru, Portugal, Paraguay	NM	NM	–
L. intricatum Boiss.	Spain, Morocco, Portugal, Mauritania, Algeria, Egypt, Saudi Arabia, Tunisia, Tunisia, Italy	NM	Seed: helminthiasis, digestive; fruit: eye diseases	Abouri et al. (2012); Ouhaddou,. et al. (2014); Boulila and Bejaoui (2015); Abdennacer et al. (2015); MPNS, 2017
L. isthmense F. Chiang	Mexico	NM	NM	–
L. leiostemum Wedd.	Chile, Peru, Mexico	NM	NM	–
L. macrodon A. Gray	US, Mexico	NM	NM	–
L. makranicum Schonebeck-Temesy	Pakistan	NM	NM	–
L. martii Sendtn.	Brazil, Cuba	NM	NM	–
L. mascarenense A.M. Venter & A.J. Scott	Mauritius, Madagascar, South Africa, Mozambique, Reunion	NM	NM	–
L. megacarpum Wiggins	Mexico	NM	NM	–
L. minimum C.L. Hitchc.	Ecuador	NM	NM	–
L. minutifolium Remy	Chile, Argentina, Mauritius	NM	NM	–
L. morongii Britton	Argentina, Paraguay, Bolivia	NM	NM	–
L. nodosum Miers	Argentina, Mexico, Paraguay, Ecuador, Venezuela, Bolivia, Peru	NM	NM	–
L. oxycarpum Dunal	South Africa, Namibia, Angola, US	NM	Used as medicine, no details	Arnold et al. (2002); MPNS, 2017

(*continued on next page*)

Table 2 (*continued*)

Species name	Distribution	Food use	Medicine use	References[a] for plant uses
L. pallidum Miers	US, Mexico	Fruit as food	Plant and root as medicine, for toothache and chickenpox	NAEB (2003); FEIS (2016); PFAF (2016); Kindscher et al. (2012); Saunders (1920); McClendon (1921); Powell (1988); Vines (1960); Hodgson (2001); Middleditch (2012); MPNS, 2017; Quattrocchi (2012)
L. parishii A. Gray	US, Mexico	Fruit as food	NM	Nabhan et al. (1982); Hodgson (2001)
L. parishii var. *modestum* (I.M. Johnst.) F. Chiang	Mexico	NM	NM	–
L. petraeum Feinbrun	Italy, Jordan; *EuroPlusMed PlantBase*	NM	NM	–
L. pilifolium C.H. Wright	South Africa, Namibia, Botswana	NM	NM	–
L. prunus-spinosa Dunal	South Africa, Namibia	NM	Used as medicine, no details	Arnold et al. (2002); MPNS, 2017
L. puberulum A. Gray	US, Mexico	NM	NM	–
L. pubitubum C.L.Hitchc.	US, Mexico	NM	NM	–
L. pumilum Dammer	South Africa, Namibia	NM	NM	–
L. rachidocladum Dunal	Chile	NM	NM	–
L. repens Speg.	Argentina, US	NM	NM	–
L. richii A. Gray	US, Mexico	Fruit as food	NM	Watson (1888); Hodgson (2001)
L. ruthenicum Murray	China, Iran, Afghanistan, India, Mexico, Pakistan, Russian, Turkmenistan, Georgia	Fruit as food	Fruit: ophthalmic, blindness (veterinary); leaf: remove blocked urine; diuretic	USDA (, 1992–, 2016); PFAF (2016); Ballabh et al. (2008); Gairola et al. (2014); MPNS, 2017
L. sandwicense A. Gray	Islands across the Pacific (Easter Island, Hawaiian Islands, Ogasawara Islands and Daitou Island)	Fruit as food	NM	PFAF (2016); Middleditch (2012)
L. schizocalyx C.H. Wright	South Africa, Botswana, Namibia, Mozambique	NM	NM	–
L. schreiteri F.A.Barkley	Argentina	NM	NM	–
L. schweinfurthii Dammer	Spain, Israel, Morocco, Greece, Portugal, Algeria, Egypt, Tunisia, Mauritania, Cyprus	NM	Leaf and fruit are used for stomach ulcer	PFAF (2016); Auda (2011); Jamous et al. (2015)
L. shawii Roem. & Schult.	Israel, Palestinian Territory, Saudi Arabia, Ethiopia, Oman, Egypt, Jordan, South Africa, Botswana, Yemen	Fruit and young shoot as food	Leaf, fruit, aerial part, and stem are used for a variety of treatments	Seifu (2004); Soltan and Zaki (2009); Cherouana et al. (2013); Ghazanfar (1994); Hassan-Abdallah et al. (2013); Trabsa et al. (2015); Chermat and Gharzouli (2015); Alkuwari et al. (2012); Sher and Alyemeni (2011); Gaweesh et al. (2015); Iwu (2014); MPNS, 2017; El-Ghazali et al. (2010); Molla et al. (2011); Dahech et al. (2013)
L. shockleyi A. Gray	US, Mexico	NM	NM	–
L. stenophyllum J. Rémy	Chile, Peru, Argentina	NM	NM	–
L. strandveldense A.M. Venter	South Africa	NM	NM	–
L. tenuispinosum S.B. Jones & W.Z. Faust	Argentina, Chile, Paraguay	NM	NM	–
L. tenuispinosum var. *friesii* (Dammer) C.H. Hitchc.	Argentina	NM	NM	–
L. tetrandrum Thunb.	Namibia, South Africa, Angola	Fruit as food	NM	Watt and Breyer-Brandwijk (1962); MPNS, 2017
L. texanum Correll	US, Mexico	NM	NM	–
L. torreyi A. Gray	US, Mexico	Fruit as food	Whole plant and root as medicine, for chickenpox and toothache	NAEB (2003); FEIS (2016); Kearney et al. (1960); Powell (1988); Vines (1960); Hodgson (2001); MPNS, 2017; Quattrocchi (2012)
L. truncatum Y.C. Wang	China	NM	Root bark as medicine *digupi*	Li et al. (2001)
L. tweedianum Griseb.	Colombia, Ecuador, Dominican, Tuks And Caicos Islands, Jamaica, Bolivia, Bahamas, Cuba, Paraguay, Virgin Island	Fruit as food	NM	Roth and Lindorf (2002)
L. verrucosum Eastw.	US	NM	NM	–
L. villosum Schinz	South Africa, Namibia, Botswana	NM	NM	–
L. vimineum Miers	Argentina, Uruguay	NM	NM	–
L. yunnanense Kuang & A.M. Lu	China	NM	NM	–

[a] Species distribution and valid plant name information sources are not included, which are extracted from: The plant list (2013); IPNI (2015); GBIF (2017); eFloras (2017); African Plant Database (Conservatory and Botanical Garden of Geneva and South African National Biodiversity Institute), 2017; EuroPlusMed PlantBase (2011); Flora of North America (2009); VicFlora (2015); Flora of Argentina (1992); Flora of Israel (2017); Flora of China (1994). If no sources are given, no references for this species' food or medicine uses.

Table 3
Main morphological characters of commonly used *Lycium* species of all continents.

Species	Berry	Flower	Stem and leaf
L. ruthenicum Murray	Purple-black, globose, or emarginate. Seeds brown.	Pedicel 5–10 mm. Calyx narrowly campanulate, 4–5 mm, regularly 2–4-lobed, lobes sparsely ciliate. Corolla pale purple, funnel form, ca. 1.2 cm; lobes oblong ovate, 1/3-1/2 as long as corolla tube, not ciliate.	0.2–1 m tall. Stems much branched. Leaves subsessile, solitary on young branches, leaf blade grayish, succulent, linear or sub-cylindric, rarely linear-oblanceolate,
L. truncatum Y.C. Wang	Red or orange-yellow. Oblong or oblong-ovoid, mucronated. Seeds orange.	Pedicel 1–1.5 cm. Calyx campanulate, 3–4 × 3 mm, 2- or 3- lobed or truncate, sometimes circumscissile and only base persistent. Corolla purple or reddish purple, tube ca. 8 mm; lobes ca. 4 mm, not ciliate.	1–1.5 m tall, sparingly armed. Branches flexible. Leaves solitary on long shoots, clustered on short shoots; leaf blade linear-lanceolate or lanceolate.
L. dasystemum Pojark.	Red, ovoid, or oblong. Seeds more than 20.	Pedicel 1–1.8 cm. Calyx campanulate, ca. 4 mm, often 2- or 3-divided halfway. Corolla purple, funnelform, 0.9–1.3 cm; tube sparingly villous inside; lobes ovate, half as long as corolla tube, ciliolate.	ca. 1.5 m tall. Stems much branched; branches grayish white, yellowish, or rarely brown-red, stout, young branches slender, elongate. Leaf blade lanceolate, oblanceolate, or broadly lanceolate.
L. barbarum L.	Red or orange-yellow, oblong or ovoid,. Seeds usually 4–20, brown-yellow, ca. 2 mm.	Pedicel 1–2 cm. Calyx campanulate, 4–5 mm, usually 2-lobed, lobes 2- or 3-toothed at apex. Corolla purple, funnelform; tube8-10 mm, obviously longer than limb and lobes; lobes 5–6 mm, spreading, margin glabrescent.	0.8–2 m tall. Stems and branches glabrous, branches thorny. Leaves solitary or fasciculate, lanceolate or long elliptic
L. cylindricum Kuang & A. M. Lu	Berry ovoid. Seeds few.	Pedicel ca.1 cm. Calyx campanulate, ca.3 × 3 mm, usually (2-or) 3-divided to halfway, lobes sometimes with irregular teeth. Corolla tube cylindric, obviously longer than lobes, 5-6mm, ca. 2.5 mm in diam.; lobes broadly ovate, ca. 4 mm, margin pubescent.	Branches inflexed, with thorns 1–3 cm. Leaves solitary or in clusters of 2 or 3 on short shoots; leaf blade lanceolate, base cuneate, apex obtuse.
L. chinense Mill.	Red, ovoid or oblong. Seeds numerous, yellow, 2.5–3 mm.	Pedicel 1–2 cm. Calyx campanulate, 3–4 mm, 3–5-divided to halfway, lobes densely ciliate. Corolla pale purple, 0.9-l.2 cm; tube funnel-form, shorter than or subequaling lobes, lobes pubescent at margin.	0.5–2 m tall. Stems much branched; branches pale gray, slender, curved or pendulous, with thorns 0.5–2 cm. Leaves solitaryor in clusters of 2–4; leaf blade ovate, rhombic, lanceolate, or linear-lanceolate.
L. yunnanense Kuang & A.M. Lu	Globose, yellow-red when ripe, with an obvious longitudinal furrow on drying. Seeds ca. 20, pale yellow, orbicular, pitted.	Pedicel 4–6 mm. Calyx campanulate, ca. 2 mm, usually 3-lobed or 3- or 4-dentate, tomentose at apex. Corolla pale blue-purple, purple, or occasionally white, funnel form, 5–7 mm; tube 3–4 mm; lobes 2–3 mm, glabrescent.	ca. 0.5 m tall. Branch lets yellow-brown, thorny at apex. Leaves solitary on long shoots, sometimes on thorns or fasciculate on tubercular short shoots; petiole short; leaf blade narrowly ovate to lanceolate, base narrowly cuneate, apex acute.
L. europaeum L.	Reddish	Flowers solitary or in c1usters of 2(−3). Calyx 2–3 mm, 5-dentate or 2-lipped. Corol1a 11–13 mm, narrowly infundibuliform, pink or white; lobes 3–4 mm. Stamens usually exserted; filaments glabrous, somewhat unequa1.	1–4 m tall; branches rigid, very spiny; spines stout. Leaves 20–50 × 3–10 mm, usually oblanceolate.
L. intricatum Boiss.	Orangc-red or black	Plant Flowers solitary or in c1usters of 2–3. Calyx 1.5–2 mm, shallowly 5-dentate. Corolla 13–18 mm, narrowly infundibuliform, blue-violet, purple, lilac, pink or white; lobes 2–3 mm. Stamens inc1uded; filaments glabrous.	0.3–2 m, much-branched, very spiny; spines stout, rigid. Leaves 3–15 × 1–6 mm, oblanceolate.
L. afrum L.	Purplish	Calyx 5–7 mm, deeply 5-dentate. Corolla 20–22 mm, subcylindrical, purplish-brown; lobes ca. 2 mm. Stamens included; filaments with dense tuft of hairs at base.	1–2 m; branches rigid, very spiny; spines stout. Leaves 10–23 × 1–2 mm, very narrowly oblanceolate.
L. berlandieri Dunal	Red, globose to ovoid, glabrous.	Solitary or in pairs, pedicels 3–20 mm long; calyx cup-shaped, 1–2 mm long, (3)4- or 5-1obed, the lobes usually shorter than the tube, glabrous except for a tuft of hair at the tip of each lobe; corolla blue, pale lavender, or ochroleucous, campanulate-funnelform, 6–7 mm long, the limb 4- or 5-1obed.	Erect shrub to 2.5 m tall, armed with needlelike spines on the younger shoots or nearly unarmed; branches somewhat crooked, glabrous. Leaves 1–3 in a fascicle, linear to elliptic-spatulate, glabrous, apex rounded to acute, margins entire, base attenuate to a short petiole or subsessile.
L. pallidum Miers	Red (drying blackish or purplish), glaucous, subglobose to ovoid, glabrous. Seeds yellowish, widely ovate to subreniform, minutely pitted.	Solitary or occasionally in pairs, pedicel 8–18 mm long; calyx campanulate, 5–9 mm long, 5-1obed, the lobes about equaling or slightly longer than the tube, glabrous; corolla greenish-white, sometimes tinged with purple, funnelform, 15–20 mm long, the limb 5-1obed.	Upright-spreading, much-branched shrubs to 20 dm tall, branches lightly pubescent to glabrous, sparingly armed with stout spines. Leaves mostly fascicled, except on young growth; blade oblanceolate or spatulate, 1–4 cm long, (3)5–15 mm wide, glabrous, apex acute to obtuse, margins entire, base attenuate; petiole 5–10 mm long.

(*continued on next page*)

Table 3 (*continued*)

Species	Berry	Flower	Stem and leaf
L. shawii Roem. & Schult.	Orange-red, 4 mm broad. Seeds ca. 1.5 mm broad, reniform, brown.	Solitary or paired, white or purple-suffused. Pedicel 3–4 mm long, pilose. Calyx narrow tubular, pilose; lobes 0.5–1 mm long, acute, pubescent. Corolla tube 10–12 mm long; lobes 2.0 mm long, acute, minutely pubescent. Filaments glabrous at the base, subexserted.	A spiny branched shrub 100–180 cm tall, shoots white-tomentose. Spines tomentose towards the base. Leaves 4–25 (−30) × 2.5–6 mm, elliptic-oblong to narrow oblong, cuneate, obtuse or acute, pilose to tomentose.

Flora of China Editorial Committee (1994), Tutin (1972), McGregor and Barkley (1986) and Ali (1980).

Levin et al., 2011; GBIF, 2017). It was first published by Linnaeus, and three species (viz. *L. europaeum*, *L. barbarum*, and *L. afrum*) were described in Species Plantarum (Linnaeus, 1753). In 1932, Hitchcock published a systematic taxonomic study on 43 *Lycium* species from the western hemisphere based on morphology (Hitchcock, 1932). Recently, molecular markers of different genome parts were used to elaborate the phylogenetic relationship within the genus as well as biogeographic events: *Lycium* originated from the Americas, and then dispersed to Africa and Eurasia; the diversity centers are the Americas and Africa (Olmstead et al., 1999; Fukuda, 2001; Miller, 2002; Yin et al., 2005; Levin and Miller, 2005; Levin et al., 2009a, 2009b; Miller, 2011; Levin et al., 2011).

According to our findings, at present ninety seven species and six varieties are recognized (Table 2). Among them, 32 are native to South America, 24 to North America, 24 to Africa, and 12 to Eurasia; two occur in Eurasia as well as Africa. *Lycium australe* is the only species endemic to Australia, and L. *sandwicense* is native to the Pacific islands. *L. carolinianum* occurs in North America as well as the Pacific islands.

Lycium species are shrubs or small trees, often with thorns on the stem and simple, entire leaves. Usually they are differentiated through the thorn on the stem, the shape and size of leaves, the corolla length, the length of stamen, colour of the fruit, the taste of the fruits, and the size and number of seeds. Morphological characters of the typical frequently used species of different continents are summarized in Table 3. However, the commercial *Lycium* products are always without these characteristic traits as they are only few parts of the plant, e.g., fruit, root bark and leaf, therefore, morphological techniques solely were not sufficient for the authentication of *Lycium* products. For example, fruits of *L. barbarum* and *L. chinense*, the two most commonly used goji, are difficult to distinguish by eye (Xin et al., 2013), which is a challenge for quality assessment in trading.

3.2. Traditional uses

3.2.1. Traditional uses worldwide

Of all 97 species, 35species and 2 varieties were found to be used as food and/or medicine (Table 2). The number of native species of the different continents used as food and medicine are shown in Fig. 1.

Although the richness of *Lycium* species differs in South America, North America, Africa and Eurasia, the numbers of species used are similar. Therefore, the species use ratios are dramatically different. In Eurasia, nine (64%) of the 14 species, and one variety, are used. While 86% of the *Lycium* species occur in the Americas and Africa, only 31% (26 species) of them are used as food and/or medicine. The Australian species as well as the two Pacific Island species are all used as food.

Of 28 species the plant parts used are the fruits, both for food and medicine, indicating that the fruit is worldwide the most commonly used plant part; of the other species also the leaves and root bark are used, and in some cases the whole plant. Leaves and root bark are usually used as medicine, while young shoots may also be prepared as food. *Lycium barbarum,* L. *chinense,* and L. *ruthenicum* are the most often reported species in the literature for China, *L. europeaum*, *L. intricatum*, and *L. shawii* for the Mediterranean and Middle East*,* L. *pallidum* for North America, and *L. afrum* for Africa. Usually the fresh or dried fruits are consumed, and the fresh leaves are cooked as food or used as tea. Of them, *L. barbarum* and *L. chinense* have been introduced as "superfood" from China to Europe, the Americas, and Australia. They are typically consumed as food supplement.

3.2.2. Use of Lycium in China over time

Today, the dried fruits and the root bark of *L. chinense* and *L. barbarum*, called *Gouqi Zi* and *Digu Pi*, are commonly used in Chinese medicine and diet (Wagner et al., 2011; Chang and So, 2015; Tan et al., 2017). Whether the same or different species have been used in the past is not easy to deduce from the historical herbals, as the species concept did not exist in earlier times; and in the older herbals, even the plant parts used were not recorded. Therefore, information has to be inferred from the Chinese characters and the plant figures in the historical herbals.

The Chinese characters "枸杞" *(gǒu qǐ)* means *Lycium*, although sometimes the word means the fruit of *Lycium* only. However, in the ancient literature the character "杞" alone was often referring to *Lycium*. "杞" was also present in the oracle bone script, a script which was used in *Shang* Dynasty (B.C.E. 1400 s to B.C.E. 1100 s), indicating that the use of *Lycium* has a long history in China. It also appeared in later scripts, like bronze inscription and seal script. The earliest record of using *Lycium* in China was found in the Book of Songs (诗经，*shī jīng*), which consisted of poems written in the *Zhou* Dynasty (B.C.E. 1100 s to B.C.E. 300 s) (Gao, 1980). In the 74 poems of the chapter *Xiaoya* (小雅，*xiǎo yǎ*), "杞" was mentioned six times. The sentences, "南山有杞 (*nán shān yǒu qǐ*)" and "言采其杞 (*yán cǎi qí qǐ*)", describe people harvesting *Lycium* plants growing in the mountains.

Records of *Lycium* in the Chinese herbals over time are listed in S1, while Fig. 2 shows *Lycium* illustrations. The earliest record of *Lycium* as medicine was in *Shennong's* Herbal (ca. C.E. 100) (Shang, 2008). The original herbal does not exist anymore, and the present edition was compiled from later citations. The text mentions the flavour, effects, common names, and habitat of *Lycium* briefly, but not the plant parts used (Li, 1954). Deduced from the given flavour, it might be the root; from the effects, it could be both fruits and roots; from the recorded common name "枸杞", it might be both fruits and roots, as some later herbals also used the same name for root and/or fruit.

In the *Jin* Dynasty (C.E. 266 − 420), *Ge Hong* (284 − 364) published two herbals, *Baopuzi* (Ge, 1995) and *Zhouhou Beiji Fang* (Ge, 1999), both of which included *Lycium*. The later was the first herbal with formulas, and *Lycium* fruit, root, and juice were recorded separately in different formulas. *Leigong Paozhi Lun* (ca. 420 − 479) (Lei, 1985), the first monograph on processing of *materia medica*, recorded the manufacture of the root bark, while the fruit decoction was used for processing another drug. *Mingyi Bielu* (Tao, 1986), published around C.E. 500, is commonly regarded as the first herbal describing the use of *Lycium* fruits; however, according to our research, *Lycium* fruits and root had already been used separately in earlier times (*Jin* Dynasty by *Ge Hong*).

Lycium was first recorded as food in *Bencaojing Jizhu* (ca. C.E. 500) (Tao, 1994). In *Xinxiu Bencao* (659) (Su, 1981) and *Shiliao Bencao* (ca. 700) (Meng, 1984), *Lycium* was also recorded as food, with several medicated diet recipes of the fruits, root, and leaves. Later, in *Qianjin Yifang* (682) (Sun, 1998), cultivation techniques of *Lycium* were described, beside its medicinal usages.

New in the *Song* Dynasty (960 − 1279) was the detailed morphological description of the plant accompanied by illustrations. *Bencao*

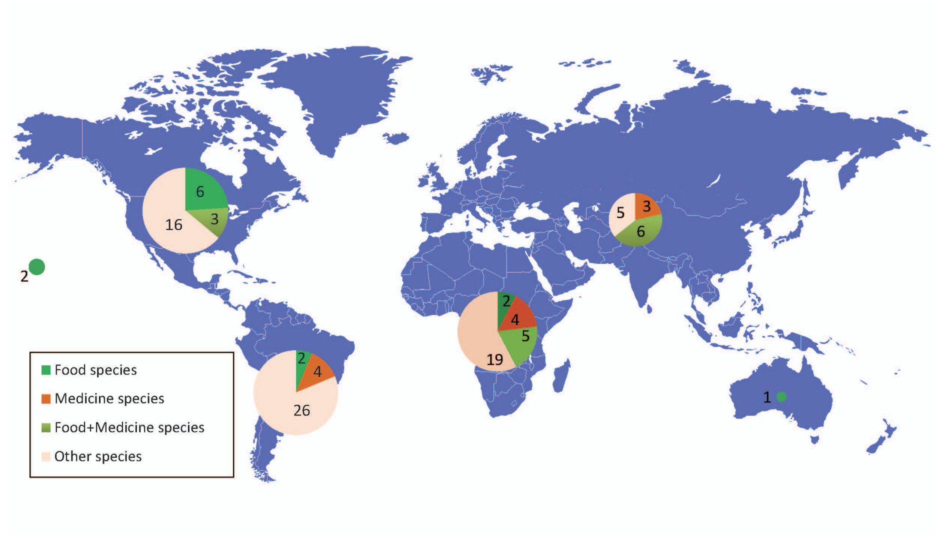

Fig. 1. *Lycium* species used as food and/or medicine on the different continents.

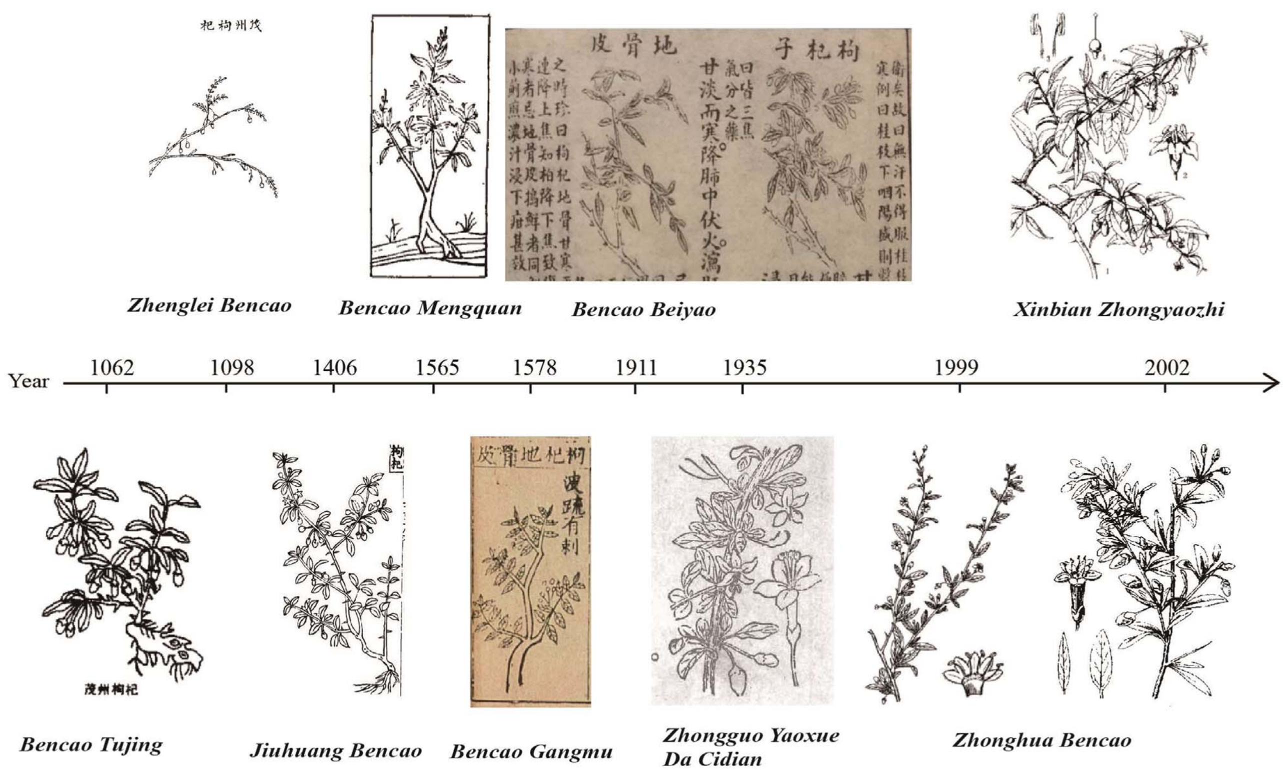

Fig. 2. Illustrations of *Lycium* in Chinese herbals over time.

Tujing (Su, 1994) and *Zhenglei Bencao* (Tang, 1982) were the most important herbals during *Song*, and *Lycium* was recorded in both.

In the *Yuan* Dynasty (1271 – 1368), the recipes of tea, porridge, and wine using the fruit or the leaves were recorded in the medicated diet monograph *Yinshan Zhengyao* (Hu, 2009).

Bencao Gangmu (1596) (Li, 1954), also known as Compendium of *Materia Medica*, discussed the habitat, the use history, manufacturing, and usage of *Lycium*, offering a review of former information as well as *Li Shizhen*'s (1518 – 1593) understanding of its use. In the *Ming* and *Qing* Dynasty (1644 – 1912), many formulas containing *Lycium* emerged and were described in various herbals. In 1935, the herbal *Zhongguo Yaoxue Da Cidian* (Chen, 1935), for the first time published the scientific name *Berberis lycium* for 枸杞. This was later found to be a misidentification, and was replaced by *Lycium*. Besides the key herbals described above, there were still many interesting ones published in different times (Chen, 1985, 1988, 2008; Du, 1975; Jiang, 1911; Kou, 1990; Liu, 1956; Lu, 1986; Ni, 2005; Wang, 1987; Wu, 1959, 1987; Yan, 1958; Yang, 1958; Zhu, 2008); as a result, these herbals conserved the food and medicine use history of *Lycium* in China.

The contemporary herbals, such as *Zhonghua Bencao* (Zhonghua Bencao Editorial Board, 1999), *Xinbian Zhongyao Zhi* (Xiao, 2002), and *Zhongyao Da Cidian* (Nanjing TCM University, 2006), refer to both L. *chinense* and L. *barbarum*. Precise botanical descriptions are provided and usages are combined with scientific findings and pharmacological evidence and guidance for use.

3.2.3. Traditional uses by Chinese ethnic minorities

In China, seven species and two varieties of the genus *Lycium* occur, of which four species have been used by different ethnic groups. We found use records for twelve of the officially recognized 55 ethnic

Table 4
Lycium spp. used in Chinese ethnic medical traditions.

Ethnic group	Distribution provinces	Species	Used parts	Indications and usages	References
藏族*Tibetan*	*Tibet, Sichuan, Yunnan, Qinghai, Gansu*	*L. barbarum*	Fruit, root, bark, leaf	Cough, *xiaoke* (similar to diabetes), dizziness, fever, gynecopathy, night sweat, lumbar genu aching and limp, leukorrhea, headache, amnesia, agrypnia, tuberculosis, spermatorrhea	Jia and Li (2005); Yu (1996)
		L. chinense	Fruit	Deficiency of the kidney and liver, anemia, cough, *xiaoke*, headache, heart hot, amnesia, agrypnia, gynecopathy	Zhonghua Bencao Editorial Board (2002); Jia and Li (2005)
		L. dasystemum	Fruit	Heart hot, gynecopathy	Jia and Li (2005)
		L. ruthenicum	Fruit	Heart diseases, gynecopathy	Dimaer (1986); Jia and Li (2005)
维吾尔族*Uighur*	*Xinjiang*	*L. barbarum/ L. chinense*	Fruit	Hyposexuality, blurry vision, neurasthenia, hyperlipidemia, oligospermia	Editorial Board (2005a)
蒙古族 *Mongol*	*Inner Mongol, Heilongjiang, Jilin, Liaoning, Xinjiang, Hebei, Qinghai*	*L. barbarum*	Fruit	*Xiaoke*, giddy dazzled, tinnitus, lumbar genu aching and limp, deficiency of the kidney and liver, fever, stasis, amenorrhea, blurry vision	Jia and Li (2005); Zhonghua Bencao Editorial Board (2004)
苗族*Miao*	*Guizhou, Hunan, Hubei, Sichuan, Yunnan, Guangxi, Hainan*	*L. chinense*	Root bark, fruit, leaf, whole plant	Fever, night sweat, dysphoric, cough and asthma, *xiaoke*, bleeding, eumatism, dizziness, swell, tuberculosis, blurry vision, deficiency of the kidney and liver, backache, fatigue, finger inflammation; medicated diet included	Editorial Board (2005b); Jia and Li (2005)
畲族*She*	*Fujian, Zhejiang*	*L. chinense*	Fruit, root, leaf, root bark	Sore throat, blurry vision, kidney deficiency and backache, male infertility, *xiaoke*, palpitation, insomnia, tears; medicated diet included	Song and Xu (2002); Jia and Li (2005)
土家族*Tujia*	*Hubei, Hunan, Chongqing, Guizhou*	*L. chinense*	Fruit, root bark	Blurred vision, giddy dazzled, spermatorrhea	Zhu et al. (2006)
景颇族*Jingpo*	*Yunnan*	*L. barbarum*	Fruit	Blurry vision, kidney deficiency, blood deficiency, neurasthenia	Jia and Li (2005)
德昂族*De'ang*	*Yunnan*	L. *barbarum*	Fruit	Blurry vision, kidney deficiency, blood deficiency, neurasthenia	Jia and Li (2005)
彝族*Yi*	*Yunnan, Guizhou, Sichuan, Guangxi*	*L. chinense*	Whole plant	Pruritus, sore and ulcer diseases	Jia and Li (2005)
朝鲜族*Korean*	*Heilongjiang, Jilin, Liaoning*	*L. chinense*	Fruit	Blurry vision, kidney deficiency, backache, neurasthenia, vomiting blood	Jia and Li (2005)
瑶族*Yao*	*Guangxi, Hunan, Yunan, Guangdong*	*L. chinense*	Root bark	Fever, night sweat, *xiaoke*, hyperlipidemia, tuberculosis	Liu (2002)
侗族*Dong*	*Guizhou, Hunan, Guangxi, Hubei*	*L. chinense*	Fruit	Gum erosion and blooding	Jia and Li (2005)

minorities of China (Table 4).

Four species have been used in Tibetan medicine, while both *L. barbarum* and *L. chinense* by the Uighurs and either of them by the other ethnic groups. Fruits as well as root bark and leaves have been commonly used. The whole plant has been used by the *Miao* and *Yi* for different purposes: *Miao* use it as a tonic, while *Yi* use it for sores and itching. The *Miao's* usages are similar to the ancient Chinese herbals' records.

In general, *Lycium* spp. have often been used for the treatments of blurry vision, fever, night sweat, kidney deficiency, cough and asthma, diabetes, heart diseases, gynecopathy, and neurasthenia. However, the *Yi* and *Dong* use them differently, i.e. the fruits of L. *chinense* are for bleeding gums, while the whole plant as antipruritic drug. They were also used as medicinal food by the *Miao* and *Yi*.

3.2.4. Comparison of traditional uses with recent pharmacological studies

Different *Lycium* species, foremost *L. barbarum* and *L. chinense*, were phytochemically analyzed and hundreds of compounds were isolated and identified (Qian et al., 2017). Bioactivities and pharmacological effects of crude extracts or compounds were assessed in pharmacological studies and it turns out that many of the traditional uses are supported by these studies. For example, the anti-aging effect of *Lycium* (probably the whole plant of *L. chinense* or *L. barbarum*) has been recorded since *Shennong's* Herbal (ca. C.E. 100); recent studies demonstrated that polysaccharides, vitamins, pigments, and crude extracts of *Lycium* fruits are benefitting age-related lesions (Bucheli et al., 2011; Li et al., 2007; Kim et al., 1997; Tao et al., 2008; Yi et al., 2013). Use for improving eyesight was mentioned in herbals as well, and Zeaxanthin, lutein, and polysaccharides were found to have retinal protection activities (Tang et al., 2011; Mi et al., 2012b; Song et al., 2012; Chu et al., 2013; Pavan et al., 2014). *Xiaoke* is a term used in ancient herbals, describing symptoms similar to present diabetes (Li et al., 2004); Studies on root bark and fruits of L. *chinense* and *L. barbarum* found that water extract, polysaccharides, organic acids, and alkaloids have an effect on lipid metabolism and oxidative restoring of diabetic animals (Ye et al., 2008; Li, 2007; Luo et al., 2004). Also, an anti-fatigue and hepatoprotective effect of *Lycium* fruits and root bark has been shown recently (Alharbi et al., 2017; Xiao et al., 2012; He et al., 2012; Cui et al., 2012), and has been recorded in herbals too.

Since *L. barbarum* and *L. chinense* are widely used species, most phytochemical and pharmacological studies have been focusing on the fruits and root bark of these two species. As a result, there are scientific evidences for their medical use, which in turn have been increasing again their popularity. Therefore, they have been adopted in pharmacopoeias of many countries and regions. For example, in the current Chinese pharmacopoeia (2015), there are 75 prescriptions containing fruits of *L. barbarum*. They were also allowed to be used as cosmetic materials in China. In contrast, only a few studies focused on other *Lycium* species, which are less widely used (Table 5).

3.3. Lycium in current pharmacopoeias

3.3.1. Lycium in recent pharmacopoeias of the world

As sources of common herbal medicines, *Lycium* species have been incorporated into several pharmacopoeias, including China, Europe, Japan, Korea, Taiwan, UK, and Vietnam (Table 6). *Lycium* has not been included in the pharmacopoeia of USA, Russia, Africa, Australia, Brazil, Argentina, Switzerland, Iran, and India.

The fruit and/or root bark of *L. barbarum* and/or *L. chinense* are the most frequently used materials mentioned in the pharmacopoeias, although the aerial part of *L. barbarum* and *L. europeaum* are recorded by the Indian Ayurveda pharmacopoeia. The European pharmacopoeia only includes the dried fruit of *L. barbarum*.

Lycium fruits (*Lycii Fructus*) and *Lycium* root bark (*Lycii Radices Cortex*) are used in several regions officially, however, the quality criteria differ. Firstly, the species used as *Lycii Fructus* differ. *Lycium*

Table 5
General bioactivities of compounds or extracts of *Lycium* spp.

Bioactivity	Compounds, extracts, or plant materials	References
Antioxidant	Flavonoids, polysaccharides, pigments, mixed extracts, fatty acid	Le et al. (2007); Li and Zhou (2007); Li et al. (2007); Bai et al. (2008); Donno et al. (2015); Benchennouf et al. (2017); Wang et al. (2010); Chung et al. (2014)
Spermatogenesis	Polysaccharides (fruit of *L. barbarum*)	Luo et al. (2014); Qian and Yu (2016); Shi et al. (2017)
Retinal protection	Zeaxanthin and/or lutein, polysaccharides	Tang et al. (2011); Mi et al. (2012b); Song et al. (2012); Chu et al. (2013); Pavan et al. (2014)
Hepatoprotective	Zeaxanthin dipalmitate, polysaccharides, betaine, flavonoids, fruit	Alharbi et al. (2017); Xiao et al. (2012); Xiao et al. (2014b); Xiao et al. (2014a); Zhang et al. (2010); Ahn et al. (2014); Ha et al. (2005)
Anti-aging	Fruit, polysaccharides, vitamins, pigments	Bucheli et al. (2011); Li et al. (2007); Kim et al. (1997); Tao et al. (2008); Yi et al. (2013)
Immunomodulation	Polysaccharides-protein complex, polysaccharides, pigments	Zhang et al. (2014); Tang et al. (2012); Chen et al. (2012); Chen et al. (2008); Chen et al. (2009a), (2009b); Xie et al. (2016); Gan et al. (2004)
Anti-tumor	Polysaccharides-protein complex, polysaccharides, mix extract, scopoletin and AA − 2βG	He et al. (2012); Cui et al. (2012); Tang et al. (2012); Hu et al. (1994); Gan et al. (2004); Liu et al. (2000)
Skin care	Polysaccharides, juice, glycoconjugate	Reeve, et al., 2010; Liang and Zhang (2007); Zhao et al. (2005)
Anti-microbial	Lyciumoside I, AcOEt-soluble fraction	Terauchi et al. (1998); Lee et al. (2005); Kim et al. (2000)
Anti-diabetic	Water extract, polysaccharides, organic acids, and alkaloids	Ye et al. (2008); Song et al. (2012); Li et al. (2004); Li (2007); Jia et al. (2003); Luo et al. (2004)
Anti-atherosclerosis	Seed oil, polysaccharides	Jiang et al. (2007); Ma et al. (2009)
Hypotensive	Water extract, polysaccharides	Kim et al. (1997); Mi et al. (2012a); Mi et al. (2012b)
Neuroprotective	Water extract, polysaccharides, alkaline extract	Ho et al. (2007); Chan et al. (2007);Ho et al. (2010); Mi et al. (2013); Wang et al. (2014)
Anti- fatigue	Polysaccharides, betaine	Wu and Guo (2015); Kim and Baek (2014)

Table 6
Lycium records in current pharmacopoeias of the world.

Region	Pharmacopoeia	Species	Used parts	Description	Identification	Examination
China	Chinese Pharmacopoeia (Pharmacopoeia Commission, 2015)	*L. barbarum*	Fruit	Harvest, process, air dry, odour, taste, macroscopic, storage, indication	Microscopic, TLC	Loss on drying ≤ 13.0%, total ash ≤ 5.0%, water extract content ≥ 55%, polysaccharides ≥ 1.8%, betaine ≥ 0.30%, heavy metals
		L. barbarum/ L. chinense	Root bark	*Yinpian*; harvest, process, odour, taste, macroscopic, storage, indication	Microscopic, TLC	Loss on drying ≤ 11%, total ash ≤ 11%, acid-insoluble ash ≤ 3%
EU	European Pharmacopoeia (9.0) (2016)	*L. barbarum*	Fruit	Dried, whole, ripe fruit	Macroscopic, microscopic, TLC	Loss on drying ≤ 13%, total ash ≤ 5%, extract content ≥ 55%
UK	British Pharmacopoeia Commision (2017)	*L. barbarum*	Fruit	Dried, whole, ripe fruit	Macroscopic, microscopic, TLC	Loss on drying ≤ 13%, total ash ≤ 5%, extract content ≥ 55%
Japan	Japanese Pharmacopoeia (17th)(2016)	*L. barbarum/ L. chinense*	Fruit	Morphologic, odour, taste, storage	TLC	Foreign matters ≤ 2%, total ash ≤ 8%, acid-insoluble ash ≤ 1%, extract content (dilute ethanol) ≥ 35%
		L. barbarum/ L. chinense	Root bark	Morphologic, odour, microscopic, taste, storage	TLC	Heavy metals, arsenic, loss on drying ≤ 11.5%, total ash ≤ 20%, acid-insoluble ash ≤ 3%, extract content (dilute ethanol) ≥ 10%
Korea	Korean Pharmacopoeia (11th)(2014)	*L. barbarum/ L. chinense*	Fruit	Morphologic, odour, taste	TLC	Foreign matters ≤ 3%, total ash ≤ 6%, betaine ≥ 0.5%.
		L. barbarum/ L. chinense	Root bark	Morphologic, microscopic	Colour test, TLC	Loss on drying ≤ 12%, foreign matters ≤ 5%, total ash ≤ 18%, acid-insoluble ash ≤ 3%, extract content(dilute ethanol) ≥ 8%
	Korean Pharmacopoeia (9th) (2007) (Korea Food and Drug Administration, 2007)	*L. barbarum/ L. chinense*	Fruit	Morphologic, odour, taste	Colour test	Foreign matters ≤ 3%, total ash ≤ 6%, betaine ≥ 0.5%.
		L. barbarum/ L. chinense	Root bark	Morphologic, microscopic	Colour test, TLC	Loss on drying ≤ 12%, foreign matters ≤ 5%, total ash ≤ 18%, acid-insoluble ash ≤ 3%, extract content(dilute ethanol) ≥ 8%
Taiwan	Taiwan TCM Pharmacopoeia (2nd)(2013)	*L. barbarum/ L. chinense*	Fruit	Macroscopic, indication, microscopic, storage	TLC	Total ash ≤ 11%, acid-insoluble ash ≤ 2%, aflatoxin ≤ 15.0 ppb, extract content (dilute ethanol ≥ 35%, water ≥40%)
		L. barbarum/ L. chinense	Root bark	Macroscopic, microscopic, storage, indication	TLC	Loss on drying ≤ 14%, total ash ≤ 15%, heavy metal ≤ 10 ppm, As ≤ 6 ppm, extract content (dilute ethanol ≥ 8%, water ≥ 10%)
Vietnam	Vietnam Pharmacopoeia (4th) (2007) (Ministry of Health, 2010)	*L. barbarum*	Fruit	Macroscopic, microscopic, process, storage, indication	TLC	Loss on drying ≤ 11.0%, total ash ≤ 5.0%, extract content ≥ 55%, foreign matters ≤ 1%
		L. barbarum/ L. chinense	Root bark	Macroscopic, microscopic, process, storage, indication	Macroscopic, microscopic, TLC	Loss on drying ≤ 11%, foreign matter ≤ 2%, total ash ≤ 11%
India	Ayurveda API (Vol. 6) (Department of Ayush New Delhi, 2008)	*L. barbarum/ L. europeaum*	Aerial part	Macroscopic, microscopic	TLC	Foreign matters ≤ 2%, total ash ≤ 15%, acid-insoluble ash ≤ 2%, extract content (dilute ethanol ≥ 4.5%, water ≥ 20%)

chinense is accepted by the pharmacopoeias of Japan, Korea, and Taiwan, but not included in the pharmacopoeias of China, Europe, UK, and Vietnam; while they are not morphologically distinguishable, practically, both of them are consumed widely. Secondly, the descriptions are different. Indications are only included in pharmacopoeias of China, Taiwan, and Vietnam; macroscopic and microscopic traits are included to different degrees. Thirdly, the identification techniques differ. Colour test as primary identification tool, which could be used for detecting some chemical groups, is only used by the Korean pharmacopoeia; TLC, which is much more specificity based on chemical fingerprint and sufficient for species differentiation, is used widely. However, it was not included in the Korean pharmacopoeia until 2012. Lastly, the quality examination indexes and their thresholds differ as well. While betaine, a bioactive compound in *Lycii Fructus*, is used as index in the pharmacopoeia of China and Korea only, contents of polysaccharides are exclusively mentioned in the Chinese one.

3.3.2. Lycium in Chinese pharmacopoeias

Since 1949, there have been 10 editions of the Chinese pharmacopoeia (Chinese Pharmacopoeia Commission, 1963, 1977, 1985, 1990, 1995, 2000, 2005, 2010, 2015). *Lycium* species described in the different editions are shown in Table 7.

Lycium was not included in the first edition of the Chinese pharmacopoeia which was published in 1953. While in 1963 *L. barbarum* and *L. chinense* were mentioned for their fruits and *L. chinense* for its root bark. This changes afterwards and *L. barbarum* was documented for its fruits while both, *L. chinense* and *L. barbarum* were used for their root barks.

The descriptions of *Lycii Fructus* and *Lycii Radices Cortex* of all editions were similar, but macroscopic traits became more and more detailed over time. Identification and examination indexes, however, changed greatly. In the 1963 edition, the identification was based on macroscopic traits only, later, microscopic, total ash, TLC, loss on drying, impurities, contents of extracts, acid-insoluble ash, and heavy metals were included in succession. The development of pharmacopoeial monographs indicates the progress of quality control of herbal medicines.

Besides the pharmacopoeia, there are still some regional medicinal criteria which are published by provinces of China. Since the environments and the customs may differ among provinces, the records are diverse. For example, in *Ningxia*, the pedicel of the fruit and leaves of *L. barbarum* are officially used; in *Xinjiang*, the fruit of *L. dasystemum* has been accepted; in *Gansu*, the root bark of *L. truncatum* has been an official source of *Lycii Radices Cortex* (Li, 2001).

Accordingly, in China the quality criteria of *Lycii Fructus* and *Lycii Radices Cortex* have experienced notable developments over time, and they vary by geographic regions.

3.3.3. Comparison of Lycium records among pharmacopoeias

As demonstrated above, the fruits and/or root bark were adopted by pharmacopoeias of many countries and regions, as well as Chinese pharmacopoeias of different times; however, the descriptions and quality requirements were different. In order to understand the relationship of these pharmacopoeias, we extracted the parameters which were used for the identification of *Lycium*. The Indian Ayurveda pharmacopoeia was not included as it describes the aerial parts of the plant as a medicine, and the Chinese pharmacopoeia 1953 was excluded since it does not record *Lycium*. The results are shown in Fig. 3.

By the parameters of fruit, pharmacopoeias are firstly categorized into two groups: those of Taiwan, Japan, and Korea are with the earlier editions of Chinese pharmacopoeia, while European pharmacopoeia 9.0 (shown as EU 2016), British Pharmacopoeia Commision (2017) (UK 2017, which is the same as EU 2016), and Vietnam pharmacopoeia IV (shown as VN 2007) are similar to the later editions of Chinese pharmacopoeias (2000–2015). The difference between KR 2007 and KR 2014 is that the later includes TLC as an identification technique, and they have a lower similarity with others. Pharmacopoeia of Taiwan and Japan are closely related and are separated from the earlier Chinese editions. The clustering also shows the development of Chinese pharmacopoeias over time: the ones before 2000 are separated from the ones since 2000; the reason is probably that the later include more examination items such as moisture and total ash.

By the data of root bark, EU 2016 and UK 2017 are separated from others since it does not adopt root bark. Pharmacopoeias of Taiwan, Japan, and Korea are in the same branch excluded from the Chinese ones. Like the result from the fruit, pharmacopoeias of Taiwan and Japan are again in the same group; VN 2007 is similar to the later Chinese ones since 2000 (except for the 2005 edition). If we consider the Chinese ones, the development is also presented by the clustering. However, the one of 2005 is grouped with the earlier ones; this may be because TLC was omitted.

Accordingly, the clustering is a practical tool to study the development of pharmacopoeia over time, as well as to reveal the relationship among pharmacopoeias of different regions.

4. Discussion

According to our study, 35 out of 97 *Lycium* species worldwide have been recorded to be used as food and / or medicine. The species use ratio in the Americas is rather low, maybe because there are many species available there. Alternatively, it would be worth to investigate the abundance of different species in the relevant regions in order to better understand the potential access to these resources. The thorny *Lycium* species are generally ignored. In order to make better use of less-used *Lycium* species, phytochemical and pharmacological studies are needed.

Only *L. barbarum* and *L. chinense* have been transformed into globally traded commodities and are marketed worldwide as a “super food”. In China, based on the Chinese name “枸杞” their use can be traced back over the last two millennia. However, identification of the plant species and plant parts used is often not possible with certainty. Nevertheless, the use of *Lycium* fruits for anti-aging, improving eyesight and nourishing can be traced back at least C.E. 500 in *Mingyi Bielu*, and these usages still continue until today in Chinese medicine.

The diversity of plant usages offers opportunities for the development of new food and or medicine products. However, challenges for the quality control will have to be overcome. According to our study, different parts of *Lycium* species are used, and both of the botanical resources and traditional knowledge are primary materials for developing traditional herbal products (Jütte et al., 2017; Tu, 2015; Ngo et al., 2013). On the other hand, those differences set obstacles with regards to the quality control of the products, and the quality criteria differ greatly among regions. Along with the popularity of the fruits of *L. barbarum* and *L. chinense*, they become global consumables. However, almost all the goji are produced in China, and the exporters have to adjust their products to meet the diverse quality requirements of different regions; the different quality criteria among regions will probably obstruct the international trading. Therefore, a relative uniform quality criterion is recommended.

In general, recent pharmacological findings on *L. barbarum* and *L. chinense* largely support traditional uses as described in ancient herbals. Especially polysaccharides, zeaxanthin dipalmitate, vitamins, betaine, and mixed extracts were reported to be responsible for anti-aging, improving eyesight, anti-fatigue effects. It is obvious that detailed pharmacognostical studies lay a solid foundation for the wide acceptance of the plants and their products. Therefore, researches also need to focus on those less well-studied species but with interesting biological activities (Yao et al., 2011; Qian et al., 2017) as potential new sources of (healthy) foods or medicines. Due to the complexity of herbal preparations, quality control using only few chemical indicators is insufficient. Instead, the metabolomic approaches need to be developed (Donno et al., 2016).

Table 7
Lycium records in Pharmacopoeias of China.

Year/ edition	species	Used part	Description	Identification	Examination
1953	NM	NM	NM	NM	NM
1963	*L. barbarum/ L. chinense*	Fruit	Harvest, process, odour, taste, indications, storage	Macroscopic	NM
	L. chinense	Root bark	Harvest, process, odour, taste, indications, storage	Macroscopic	NM
1977	*L. barbarum*	Fruit	Harvest, process, odour, taste, macroscopic, indications, storage	NM	NM
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, indications, storage	Microscopic	NM
1985	*L. barbarum*	Fruit	Harvest, process, odour, taste, macroscopic, indications, storage	NM	Foreign matter ≤ 1%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	NM
1990	*L. barbarum*	Fruit	Harvest, process, odour, taste, macroscopic, indications, storage	NM	Foreign matter ≤ 1%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	Total ash ≤ 11%
1995	*L. barbarum*	Fruit	Harvest, process, sun dry or air dry, odour, taste, macroscopic, indications, storage	NM	Foreign matter ≤ 2%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	Total ash ≤ 11%
2000	*L. barbarum*	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	TLC	Loss on drying ≤ 13.0%, total ash ≤ 5.0%, foreign matters ≤ 0.5%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Total ash ≤ 12%
2005	*L. barbarum*	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Loss on drying ≤ 13.0%, total ash ≤ 5.0%, water extract content ≥ 55%, polysaccharides ≥ 1.8%, betaine ≥ 0.30%
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic	Total ash ≤ 11%
2010	*L. barbarum*	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Loss on drying ≤ 13.0%, total ash ≤ 5.0%, water extract content ≥ 55%, polysaccharides ≥1.8%, betaine ≥ 0.30%, heavy metals
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Loss on drying ≤ 14%, total ash ≤ 10%, acid-insoluble ash ≤ 3%
2015	*L. barbarum*	Fruit	Harvest, process, air dry, odour, taste, macroscopic, indications, storage	Microscopic, TLC	Loss on drying ≤ 13.0%, total ash ≤ 5.0%, water extract content ≥ 55%, polysaccharides ≥ 1.8%, betaine ≥ 0.30%, heavy metals
	L. barbarum/ L. chinense	Root bark	Harvest, process, odour, taste, macroscopic, indication, storage	Microscopic, TLC	Loss on drying ≤ 11%, total ash ≤ 11%, acid-insoluble ash ≤ 3%

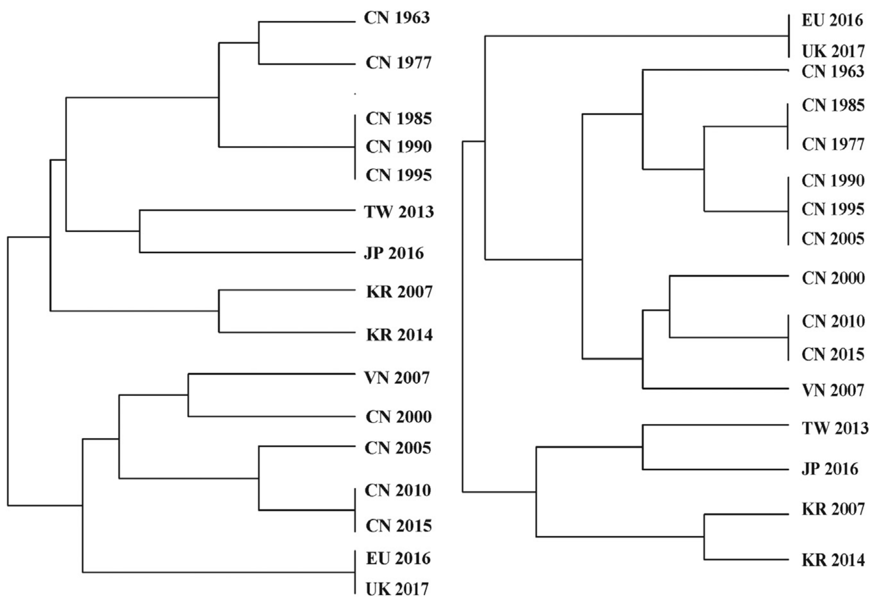

Fig. 3. Clustering based on parameters of *Lycium* fruit (left) and *Lycium* root bark (right) in different pharmacopoeias.

Historical documentary evidences are good basis for ethnobotanical study (Heinrich et al., 2006, 2012; Jütte et al., 2017). The historical continuity of Chinese medical herbals showcase the evolution of peoples' medical knowledge and offer ideas for treatment options for current diseases. In this study, the use history of *Lycium* in China was mapped out using the herbals, and some of the reported effects involved, such as anti-aging, retinal protection, and anti-fatigue, have been demonstrated experimentally. However, there are gaps between the descriptions in Chinese herbals and modern concepts: 1) the species are often not properly described as most of them were not written by botanists but doctors; 2) the terms of diseases and the description of symptoms are difficult to understand because of the difference of medical concepts; 3) the herbals contain historical "clinical data" and both the right and inaccurate information are included. As a result, the herbals are important sources of medicinal and nutritional researches, but they need to be used dialectically.

5. Conclusions

A comprehensive understanding of a species' characteristics, which includes taxonomy, geographic distribution, traditional use, phytochemistry, pharmacology, knowledge evolution, and quality control, is indispensable for finding new sources for food and/or medicine. This article highlights the need for a very sound understanding of the multicontextual basis of what is commonly termed a species 'traditional use'. The research approach used had to be transdisciplinary and the integration of historical, modern ethnobotanical, botanical, phytochemical and pharmacological data has enabled a much more detailed understanding of the genus as a whole and its wider potential. It also highlights that the focus so far has only been on two species and that the genus can potentially yield a wide range of other products with different properties.

This research has relied heavily on historical documentary evidences and such sources are good starting points for ethnopharmacological studies. In the present work, a set of time-continuous historical herbals of Chinese medicine generated a database on its usage and has allowed us to better understand the evolution of knowledge about *Lycium*. Hopefully, this ethnobotanical review incorporating both space and time dimensions will serve as a model for studying traditional food or medicine plants.

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Author contributions

All authors developed the concept for the study; R. Yao conducted the literature survey and drafted the paper. C.S. Weckerle and M. Heinrich supervised the work, and revised the manuscript.

Appendix A. Supporting information

Supplementary data associated with this article can be found in the online version at http://dx.doi.org/10.1016/j.jep.2017.10.010.

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CHAPTER 2

Quality variation of goji (fruits of *Lycium* spp.) in China: A comparative morphological and metabolomic analysis

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Goji from different climatic regions are being traded at the Goji Distribution Centre in Zhongning County of Ningxia; photo was taken on 19th July, 2015.

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Quality Variation of Goji (Fruits of *Lycium* spp.) in China: A Comparative Morphological and Metabolomic Analysis

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Goji (fruits of *Lycium barbarum* L. and *L. chinense* Mill.) has been used in China as food and medicine for millennia, and globally has been consumed increasingly as a healthy food. Ningxia, with a semi-arid climate, always had the reputation of producing best goji quality (*daodi* area). Recently, the increasing market demand pushed the cultivation into new regions with different climates. We therefore ask: How does goji quality differ among production areas of various climatic regions? Historical records are used to trace the spread of goji production in China over time. Quality measurements of 51 samples were correlated with the four main production areas in China: monsoon (Hebei), semi-arid (Ningxia, Gansu, and Inner Mongolia), plateau (Qinghai) and arid regions (Xinjiang). We include morphological characteristics, sugar and polysaccharide content, antioxidant activity, and metabolomic profiling to compare goji among climatic regions. Goji cultivation probably began in the East (Hebei) of China around 100 CE and later shifted westward to the semi-arid regions. Goji from monsoon, plateau and arid regions differ according to its fruit morphology, whereas semi-arid goji cannot be separated from the other regions. *L. chinense* fruits, which are exclusively cultivated in Hebei (monsoon), are significantly lighter, smaller and brighter in color, while the heaviest and largest fruits (*L. barbarum*) stem from the plateau. The metabolomic profiling separates the two species but not the regions of cultivation. *Lycium chinense* and samples from the semi-arid regions have significantly ($p < 0.01$) lower sugar contents and *L. chinense* shows the highest antioxidant activity. Our results do not justify superiority of a specific production area over other areas. Instead it will be essential to distinguish goji from different regions based on the specific morphological and chemical traits with the aim to understand what its intended uses are.

Keywords: *Lycium*, goji, metabolomics, HPTLC, ^{1}H NMR, climatic region, chemometric

Abbreviations: ChP, Chinese Pharmacopoeia; EP, European Pharmacopoeia; HPTLC, High Performance Thin Layer Chromatography; NMR, nuclear magnetic resonance; PCA, principal component analysis; SE, standard error.

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INTRODUCTION

In Chinese medicine, "*daodi* medicinal material" (道地药材, *dào dì yào cái*) spells out the relationship between medicinal material and one specific region with its traditional culture, human behaviors, and environmental conditions. Generally speaking, a *daodi* herbal medicine is derived from specific germplasm, a specific geographic location, and cultivated and processed with particular technologies with a long history. It is commonly recognized to be of high, stable quality, and reliable efficacy (based on traditional medicinal concepts), and has a longstanding, good reputation (Guo, 2004; Xiao et al., 2009; Zhao et al., 2012). However, nowadays the *daodi* concept is often not accepted as sufficient for defining good quality and as evidence for a species' therapeutic benefits. The prevalence of herbal medicines for health purposes, such as food supplements and neutraceuticals, stimulates the botanical products market (Dillard and German, 2000; Lachance and Das, 2007; Knöss and Chinou, 2012; Hilton, 2016). For the widely consumed herbal medicines, *daodi* areas cannot produce enough plant material to meet the market demands; therefore, new cultivation areas are developed. Therefore, studies on the authentication of a species in the context of the production areas, quality criteria, as well as standardized plantation and processing techniques are increasingly important (Xiao et al., 2009). However, the constitutions of herbal medicines are influenced by a wide range of factors, such as meteorological conditions, environment and processing method (Donno et al., 2012, 2016b; Zhang et al., 2012; Qi et al., 2016; Shen et al., 2016). As a result, the authentication and quality control of botanical products become even more difficult.

This is the case for goji (*Lycii frutus*, fruits of *Lycium barbarum* L. and *L. chinense* Mill.), which has been used as health food and traditional medicine for millennia in China and other regions of the world (Yao et al., 2018a). Recently, numerous phytochemical and pharmacological studies focus on its health benefits, and support its use as functional food (often sold under the marketing concept of an alleged "superfood") (Yao et al., 2011; Chang and So, 2015; Qian et al., 2017).

While Ningxia is recognized as the *daodi* region of goji, increasing market demands pushed the cultivation into new regions in China and goji fields now stretch over different geographical and climatic environments between 82°E and 115°E, 30°N and 45°N (Xu et al., 2014; Cao and Wu, 2015). These include temperate monsoon climate (Hebei), temperate continental semi-arid climate (Ningxia, Gansu, and Inner Mongolia), plateau continental climate (Qinghai), and continental arid climate (Xinjiang). These different environmental conditions influence both the appearance and the metabolite profile of goji (e.g., amount of polysaccharides, flavonoids, betaine, and carotenoids) (Zhang et al., 2012; Lin, 2013; Liu X.X. et al., 2015; Shen et al., 2016). Furthermore, different species and cultivars are cultivated in different areas: *L. barbarum* cultivars (e.g., *Ningqi* series) are widely cultivated while *L. chinense* is only cultivated in Hebei (Cao and Wu, 2015). In recent years, many of the new cultivation areas with different climates have been officially labeled as "home of goji" (枸杞之乡, *gǒu qǐ zhī xiāng*) by different governmental bodies, a category distinct from *daodi* (**Figure 1**). This label stands for standardized production including growing it on large-scale fields and for high quality products.

FIGURE 1 | Goji cultivation areas and "home of goji" in China. Up to 2015, the total cultivation area was estimated to be 1500 km^2, and nine cultivation areas were labeled as "home of goji."

Thus, both "*daodi*" and "home of goji" stand for good quality connected with a specific region. As these regions have different climates, one must ask*: How does goji differ among production areas of distinct climatic regions?*

Traditionally, good goji quality was defined as: Large berries with red color, mild texture, few seeds, and sweet taste (Chinese Pharmacopoeia Commission, 1963). Such morphological characteristics are largely used by goji traders for sensory identification. Recently, goji quality assessment also has relied on a few marker compounds, such as polysaccharides and betaine (Korea Food and Drug Administration, 2014; Chinese Pharmacopoeia Commission, 2015a), and HPTLC flavonoid fingerprint for species identification (European Directorate for the Quality of Medicines and Healthcare, 2017). Since berries from different species and cultivars are anatomically and morphologically similar, molecular identification, infrared spectroscopy, chemical fingerprint, and bioactivity are also used for identification or evaluation (Zhang et al., 2001, 2016; Yao et al., 2010; Xin et al., 2013; Donno et al., 2015).

In our study, we also include metabolomic profiling for quality assessment, which has not been used for goji yet. Chemometric approaches with chromatographic fingerprinting are known to be effective metabolomic methods for quality control of herbal medicine (Donno et al., 2016a; Guo et al., 2017; Liu et al., 2017; Martinez-Frances et al., 2017). Bioactivity-based characteristics are good quality indicators too, as they are pharmacologically relevant (Walch et al., 2011; Liu et al., 2017). Since goji was reported to have health protective effects against oxidative stress, and was recommended as a natural antioxidant (Donno et al., 2015; Benchennouf et al., 2017), we assume that antioxidant effects are an adequate quality marker.

Our research questions / objectives and the resulting research strategy are:

> Does goji from climatically different production areas show different quality characteristics? Can we correlate

quality measurements with specific production areas? We focus on the following quality measurements, which are then correlated with the four main production areas: fruit morphology, sugar and polysaccharide contents, antioxidant activity, and metabolomic profiling.

At least two species are traded widely as goji, requiring an understanding of the species similarities and differences. For this comparative characterisation and identification we use HPTLC.

To understand the spread of goji production in China over time we use historical records.

MATERIALS AND METHODS

Historical Literature Study

Information about historic goji cultivation areas was retrieved from the 32 ancient Chinese herbals used in our previous study (Yao et al., 2018a); and the toponymes were cross-linked to contemporary maps. For developments in recent decades, the search engine Baidu[1] was employed, using "中国枸杞之乡" ("home of Chinese goji," *zhōng guó gǒu qǐ zhī xiāng*) as keyword; Then, the source information was tracked down. All data were integrated and maps were generated with R 3.4.1 and the R package REmap (Liang, 2015; R Core Team, 2017).

Plant Material

Fieldwork was carried out by the first author for several weeks between August 2014 and September 2016 and goji samples were collected in the main production areas in China: Ningxia, Qinghai, Xinjiang, and Hebei. In total 51 fruit samples of *L. barbarum* and *L. chinense* were collected directly from the farmers, or were offered by institutions (Ningxia Qixiang Biological Foodstuff Co., Ltd., Hebei Julu Shengying Gouqi Co., Ltd., Xinjiang Gouqi Development and Management Center of Jinghe County, Jinghe Guokang Gouqi Specialized Farmers Cooperatives), or were bought in the Zhongning Goji Distribution Center, Julu Goji Yinhua Market, Xinjiang Jinghe Goji Market, Chengdu Hehuachi Chinese Herbal Medicine Market, and An'guo Chinese Herbal Medicine Market. This includes *L. chinense*: ten samples from the monsoon region; and *L. barbarum*: 25 from the semi-arid region, nine from the plateau region, and seven from the arid region. An authenticated reference standard sample of *L. barbarum* fruits was bought from the National Institute of Food and Drug Control of China, batch No. 121072-201410. Fruits with voucher specimens were collected in Zhongning County of Ningxia, Julu County of Hebei, and the National Gouqi Germplasm Garden in Yinchuan City of Ningxia. Totally, 24 specimens are deposited in the herbarium of the University of Zürich and ETH Zürich (Z+ZT).

Morphological Identification

Identification of the specimens is based on the Flora of China (Wu et al., 1994) and *Lycium* specimens from the China National Herbarium (PE): The barcode No. of the referred specimens are 01882829, 00633675, 00633726, 00031413, 00031311, 00031382, 01432314, 00031381. Fruits of the following two specimens were used as reference for HPTLC fingerprint analysis: Z.000106520 (*L. chinense* Miller) and Z. 000106530 (*L. barbarum* L.).

Chemicals and Reagents

Methanol (HPLC Ultra) was purchased from Roth; Ethyl acetate (98%+), Formic acid (99.5%), Glacial acetic acid (99.5%) were bought from Acros Organics; Dichloromethane (DCM) (99.9%+), Dimethylsulfoxide-d6 (DMSO-d_6), 4,4-dimethyl-4-silapentane-1-sulfonic acid (DSS), and Trifluoroacetic acid (TFA) (99%) were obtained from Sigma; all reagents and chemicals are of analytical grade. NP reagent: 1 g Diphenylborinic acid aminoethylester in 200 ml Ethyl acetate. PEG reagent: 10 g Polyethyleneglycol-400 in 200 ml Dichloromethane.

Morphological Measurements

Fruits were placed in a drying oven at 60°C for 6 h then were cooled down overnight. High-resolution images of the fruits were obtained by using an image scanner (Epson Perfection V750 Pro, United States). Length and width of each fruit were measured in Adobe Photoshop by using the ruler tool, which was done by selecting a smallest rectangle to cover the fruit outline and recording the length and width of the corresponding rectangle. Color parameters of the fruit images were represented by RGB values which were measured as follows: A smooth and clean area on the fruit image was selected such that its color was representative of the whole fruit; then, the RGB value of this area was read from the information toolbox using the color sampler tool in Photoshop.

For weight measurement 50 fruits per sample were randomly selected and weighed. This was repeated three times per sample. If the difference between any two of the three measurements was over 5.0%, another batch of 50 fruits was weighed. The process was repeated until there were three measurements with differences below 5.0%.

Data were analyzed with R 3.4.1 in RStudio 1.0.153. R packages of ggplot2, multcomp, and MASS were used (Venables and Ripley, 2002; Hothorn et al., 2008; Wickham, 2009; R Core Team, 2017).

HPTLC Fingerprint Analysis

HPTLC fingerprint analysis was applied on all samples based on the monograph of *Lycii fructus* (04/2015:2612) in the European Pharmacopoeia 9.0 (European Directorate for the Quality of Medicines and Healthcare, 2017), with slight modification.

Test solution was prepared as follows: To 0.10 g of powdered goji, 7 ml of water were added and sonicated for 10 min at room temperature. After centrifugation (5000 r/min for 5 min), 4 ml of the supernatant was loaded onto a 6 ml solid phase extract (SPE) C18 cartridge (Strata C18-E, Phenomenex, United States) that had been pre-treated first with 3 ml of methanol, dried, and then with 3 ml of water (not dried). The loaded and dried cartridge was twice washed with 1 ml of water-methanol (90:10) and dried. The test solution was obtained by elution of the cartridge with 1 ml of methanol. During loading, clean-up and elution the flow rate of the solvent should not exceed 120 drops per minute.

[1] http://www.baidu.com

A CAMAG HPTLC system (Muttenz, Switzerland) was employed, with an automatic TLC sampler 4 (AST 4) for application, an automatic developing chamber 2 (ADC 2) for developing, a chromatogram immersion device III for derivatization, a TLC plate heater III, a TLC visualizer 2 for imaging and a software visionCATS 2.0 for data analysis. Strata C18-E (55 μm, 70 A, 500 mg/6 ml) solid phase extraction cartridges from phenomenex were used for sample preparation, and the plates used were HPTLC glass 20 cm × 10 cm, Si 60 F_{254} (Merck, United States).

Application parameters were: Spray gas = air; Sample solvent type = methanol; filling speed = 15 μl/s; predosage volume = 200 nl; retraction volume = 200 nl; rinsing cycles/vacuum = 1/4 s; filling cycles/vacuum = 1/0 s; rinsing solvent name = methanol; nozzle temperature = unheated; rack in use = standard. And 10 μL of test solution and 2 μl of reference solution were applied as bands of 8.0 mm, while the application position was 8.0 mm from the lower edge of the plate; first position X: 20.0 mm, distance: 11.4 mm.

Developing conditions were: Humidity control: 33% with $MgCl_2$; saturation: 20 min with filter paper; developing distance from application position/lower edge: 62/70 mm; developing solvent: Ethyl acetate, water, acetic acid, formic acid 100:27:11:11; developing time: 20 min; plate drying: 5 min.

Derivatization was done with chromatogram immersion device III at speed of 5 with time of 0 s. Derivatization reagents: NP regent and PEG regent. The developed plate was preheated at 100°C for 3 min; the warm plate was treated with NP reagent, and photographed when dry; treatment with PEG reagent followed, and pictures were taken after 5 min. Images were taken at conditions of "auto capture, Auto, level 85%, Band." The images were analyzed with visionCATS 2.0.

^{1}H NMR Profiling

For the metabolomic profiling of all samples, the method of Booker et al. (2016) was modified: 0.0500 g of goji (fine powder, freeze dried) in a 1.5 ml centrifuge tube with 0.900 ml DMSO-d_6 and 0.100 ml of 0.100 g/ml DSS solution. After vortexing (Rodamixer, United Kingdom) for 30 s, the samples were sonicated in an ultrasound bath (XB22, Fisher, United Kingdom) for 20 min. Then, the solution was centrifuged for 5 min at 14,000 rpm (EBA 21, Hettich, Germany). Supernatant (0.600 ml) was transferred into a 5 mm diameter NMR spectroscopy tube for ^{1}H NMR analysis (AV 500, Bruker BioSpin GmbH, Germany). The parameters were: solvent = DMSO, temperature = 300, experiment = 1D, number of scans = 128, pulse width = 13.9, acquisition time = 3.172, spectrometer frequency = 500.13, nucleus = ^{1}H.

Since the samples could not be analyzed in one group, they were separated into five batches. To ensure the stability of the measurement, in every batch we took one sample for triplicated extraction and testing; one of the samples was analyzed in each batch.

The data were processed by MestReNova 9.0 (Mestrelab Research S.L., Spain). After phase correction and baseline correction, we calibrated the chemical shift reference by adjusting the first right DSS peak at 0.000 ppm. The spectrum was normalized by setting the total area of peaks (δ = 10.00–0.000 ppm) to 100.000. The binning function was applied to integrate the peak area by small buckets (0.040 ppm) with the method of "sum." The data were exported as a ".csv" file and analyzed with R and R package ggplot2 (Wickham, 2009; R Core Team, 2017).

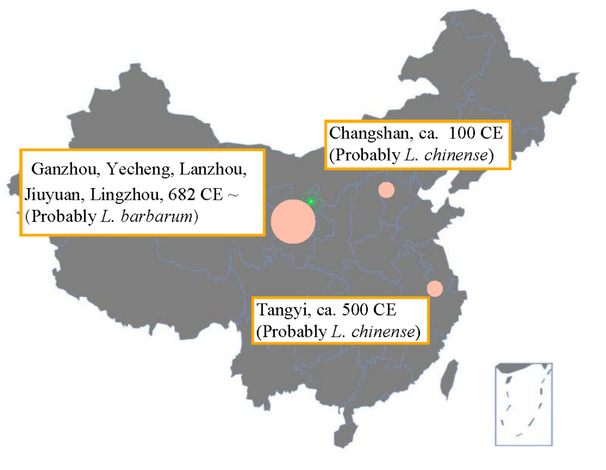

FIGURE 2 | Goji cultivation map according to Chinese historical herbals (100 CE - 700 CE). The map was produced based on the historical maps of the Han and Tang Dynasty. Data are from *Shennong*'s herbal (ca. 100 CE), Mingyi Bielu (ca. 500 CE), and Qianjin Yifang (682 CE). Later, good quality goji was consistently ascribed to the semi-arid region.

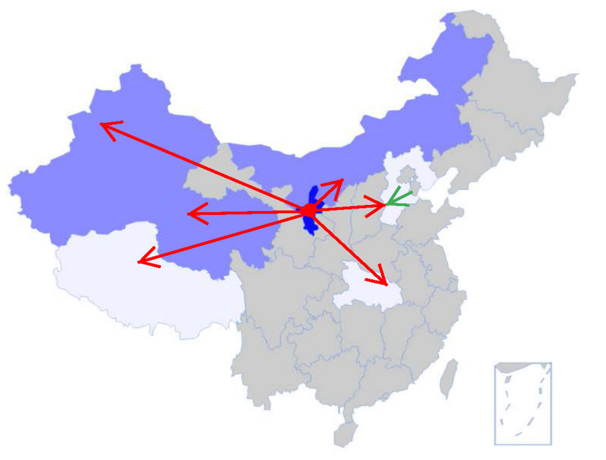

FIGURE 3 | Development of goji cultivation since 1960s. Cultivars of *L. barbarum* were introduced in large scale from Ningxia (dark blue) to Inner Mongolia, Xinjiang, Qinghai (bright blue); and in lesser degree into Tibet, Hubei, and Hebei (white) (red arrows). The green arrow shows the expansion route of *L. chinense* westward within Hebei.

Contents of Hydrolyzed Sugars and Polysaccharides

Moisture of all samples was measured according to the method No. 0831 of the Chinese Pharmacopoeia (Chinese Pharmacopoeia Commission, 2015b). 20 g of fruits were placed in an open aluminum box (with cover) into a drying oven at 105°C. After 4 h, the box was weighed every half hour until the weight no longer decreased, then all the dried samples were weighed and the moisture content calculated.

Hydrolyzed sugars were extracted according to the monograph of Xanthan Gum (04/2009: 1277) of the European Pharmacopoeia 9.0 (European Directorate for the Quality of Medicines, and Healthcare, 2017). To 0.050 g of goji powder in a thick-walled centrifuge tube, 2.0 ml of a 230.0 g/L solution of TFA was added, and shacked vigorously. The test tube was closed and heated at 120°C for 1 h. The hydrolysate was centrifuged, and 1.0 ml of the clear supernatant liquid transferred into a 10.0 ml flask, and 5.0 ml of water was added to obtain the test solution. Polysaccharides were extracted according to the monograph of *Lycii fructus* in the Chinese Pharmacopoeia (Chinese Pharmacopoeia Commission, 2010; Chinese Pharmacopoeia Commission, 2015a).

The contents of hydrolyzed sugars and polysaccharides were measured with the phenol-sulphuric acid method (Zou et al., 2011): glucose was used to plot a standard curve, and the final result was corrected with the moisture of the samples.

Antioxidant Activity

Fifteen samples (three from monsoon, eight from semi-arid, two from plateau, and two from arid) were randomly selected, and each of them was prepared as follows: Fifty grams of fruits were extracted with 1000 ml of 95% ethanol, followed by 50% ethanol, and hot water. The supernatants were collected separately and concentrated with a rotary evaporator before frozen and dried in a freeze dryer (Zou et al., 2014). The extracts were named as A-95% EtOH, B-50% EtOH, and C-H_2O, separately. Another 50.0 g of goji was extracted with 1000 ml of boiling water for the aqueous extract (Zou et al., 2014), and processed as above, and the extract was named as D-H_2O.

The antioxidant activities of the extracts were tested using a modified ABTS method (Li et al., 2012). The obtained extracts were solved in 95% EtOH in the ratio: 1000.0, 800.0, 600.0, 400.0, and 200.0 μg/ml. Quercetin was used as positive control. IC_{50} values, the concentration of 50% radical-scavenging effect, were calculated by linear regression. Data were analyzed with R and package multcomp (Hothorn et al., 2008; R Core Team, 2017).

RESULTS AND DISCUSSION

Ancient and Current Goji Distribution in China

The ancient distribution of goji cultivation areas is shown in **Figure 2**. The earliest goji record was found in the *Shennong*'s Herbal Classic describing that around 100 CE it grew in Changshan (now Hebei) during the Han Dynasty (Shang, 2008). According to the ascribed bitter taste we assume that they were describing *L. chinense*. Around 500 CE, goji was recorded to appear widely around Tangyi at south of Hebei (Su, 1981; Tao, 1986). Sun Simiao recorded 682 CE that goji grew in the semi-arid climatic region in Ganzhou, Yecheng, Lanzhou, Jiuyuan, and Lingzhou; he also described its cultivation technology and the sweet taste and superior quality of the berries compared to other regions (Sun, 1997). Very probably he referred to *L. barbarum*. From the Song Dynasty (10th-13th century) onward, goji was mentioned widely, and most records agreed that goji (probably *L. barbarum*) from semi-arid regions had the best quality (Wu, 1959; Tang, 1982; Li, 2003). Overall, goji cultivation seems to have begun in the East (Changshan) and later shifted westward to the semi-arid regions.

Since the 1960s, goji was introduced further west and north to the Inner Mongolia (semi-arid region), Qinghai (plateau region), and Xinjiang (arid region); in Hebei, cultivation shifted westward from Jinghai to Julu and Qinglong County (**Figure 3**), while *L. barbarum* was also introduced for cultivation (Cao and Wu, 2015). Since the Chinese pharmacopoeia exclusively accepts *L. barbarum* as medicinal goji (Chinese Pharmacopoeia Commission, 2015a), *L. chinense* is only locally cultivated. The fruits of *L. chinense* are sparsely consumed in China, but in Japan and Korea, the two species are used interchangeably (Korea Food and Drug Administration, 2014; Japanese Pharmacopoeia Editorial Committee, 2016).

In 1961, Zhongning County of Ningxia was assigned to be the unique national plantation for goji by the State Council of the P. R. China (Su, 2002). At a small scale, goji was also introduced to Hubei and Tibet in the 1970s and 2000s, respectively (Cao and Wu, 2015).

In recent years, the increase of goji consumption stimulated a drastic increase of goji cultivation and the total cultivation area in China now exceeds 1500 km^2. As shown in **Table 1**, up to 2017, eight "home of Chinese goji" labels and one "home of Hebei goji" were attributed to cultivation areas in different climatic regions. The latter is probably due to the long cultivation history of the area and not to the size of production area which covers only around 4 km^2. Both titles indicate the reputation of high quality products.

HPTLC Fingerprint for Species Identification

Fruits of *L. barbarum* and *L. chinense* cannot be distinguished readily (Xin et al., 2013). We therefore checked and confirmed the identity of all samples with HPTLC fingerprinting (**Figure 4**).

Flavonoids fingerprints of the same species are highly similar, indicating their chemical similarity, while fingerprints of the two species differ. The most obvious differences are: *L. barbarum* shows a yellow zone at $Rf = 0.32 \sim 0.35$, which is rutin; while *L. chinense* lacks rutin, but has a yellow zone at $Rf = 0.25 \sim 0.27$, which might be a derivative of rutin.

Morphological Characteristics

Length, width, length/width ratio, and redness are intuitive criteria used by stakeholders (cultivators, middlemen, and manufacturers) to evaluate goji quality. **Figure 5A** shows an image of goji. Samples from the semi-arid region cannot be separated morphologically from the other regions and were excluded for further analysis (**Figures 5G,H**). According to a quadratic discriminant analysis (QDA), the within training data

TABLE 1 | An overview of "home of goji" in China until 2017*.

Climatic region	Province	Cultivation location	Issued tittle	Issue department	Issue time
Monsoon	Hebei	Julu	Home of Hebei goji	HBG	2002
Semi-arid	Ningxia	Ningxia	Home of Chinese goji	SC	1995
		Zhongning		EFA	2000
	Inner	Hangjinhou Qi		SFA	2004
	Mongolia	Wulateqian Qi		EFA	2013
Plateau	Qinghai	Nuomuhong Farm		EFA	2015
Arid	Xinjiang	Jinghe		MA	1998
		Nongwu Shi		SFA	2001
		Jinghe		SFA	2004

**Semi-arid, temperate continental semi-arid climate; Arid, continental arid climate; Plateau, plateau continental climate; Monsoon, temperate monsoon climate. SC, the State Council of the P. R. China; MA, Ministry of Agriculture of P.R. China; SFA, State Forestry Administration of P.R. China; EFA, Economic Forest Association of China; HBG, Government of Hebei Province. (Cao and Wu, 2015; State Forestry Administration of P.R. China, 2017).*

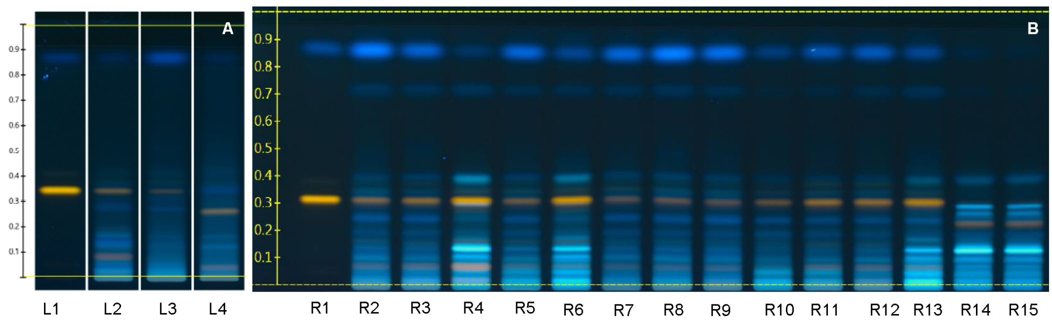

FIGURE 4 | Goji flavonoid fingerprint by HPTLC. **(A)** References (L1, Rutin Rf = 0.34 and Scopletin Rf = 0.88; L2, *Lycii fructus* standard reference; L3, voucher specimen of *L. barbarum*; L4, voucher specimen of *L. chinense*); **(B)** Samples (R1, Rutin and Scopletin; R2 – R13, samples of *L. barbarum*; R14 – R15, samples of *L. chinense*). Derivatization was done with NP regent and PEG regent, and images were taken at 366 nm.

classification error rate is 12.8%. Samples from monsoon, plateau and arid regions differ in their morphology (**Figure 5G**).

Overall, *L. chinense* fruit samples from Hebei are significantly lighter, smaller and brighter in color (**Figures 5B–D,F**), while the heaviest and largest fruits stem from the plateau (**Figures 5C,D**). In the plateau and arid region, the drastic temperature fluctuation between day and night seem to have a positive influence on fruit weight (Qi et al., 2016).

Commercial goji are normally categorized into six grades depending on the number of fruits per 50 g. The best grade contains 180–200 fruits per 50 g, and the lowest grade 980 fruits. **Figure 5B** shows a weight comparison of goji from different climatic regions.

The shape of goji fruits, which is measured by length/width ratio, differs significantly ($p < 0.01$) among regions (**Figure 5E**). Goji from the plateau region has the largest, while the arid region shows the smallest ratio. Goji from the plateau appears to be elongated oval or lanceolate, while samples from other regions are of shorter oval shape. This character is often used by stakeholders to identify the origin of goji. In the market, goji with larger berries tend to get higher prices. Therefore, farmers of the plateau region often press goji before selling it.

Redness is attractive for most consumers, unless it is too bright which may hint at sulfur treatment. In the monsoon region it is generally difficult to dry goji in the sun, and therefore sulfur fumigation is often applied to avoid degradation due to moisture. As a result, Hebei goji tends to be bright red in color. In the arid region sulfur is rarely used and goji redness is lower. The use of sulfur in semi-arid and plateau regions depends on the weather, whereas sulfur is applied in case of rain or lack of sun. In recent years, artificial drying rooms have been used increasingly to decrease the use of sulfur.

Fruit traits of goji are affected by temperature, humidity, duration of sunshine and altitude (Lin, 2013; Qi et al., 2016). However, fruit morphology may differ even within the same climatic region (Lei et al., 2013). Moreover, the drying process has an impact on the color (Ma et al., 2008). Goji from the semi-arid region, especially Ningxia, is recognized as having higher quality compared to other regions. However, from our morphological analysis goji berries from the semi-arid region are not distinguishable from berries from other regions and, therefore, it is possible to wrongly label goji from different regions as "Ningxia goji" to charge high prices.

^{1}H NMR Based Metabolomic Profiling

With the metabolomic profiling we were able to separate the two species but not the samples from different cultivation regions (**Figure 6**). Differentiation of several other species according to their metabolomic profiles has been done before, e.g., *Rhodiola*

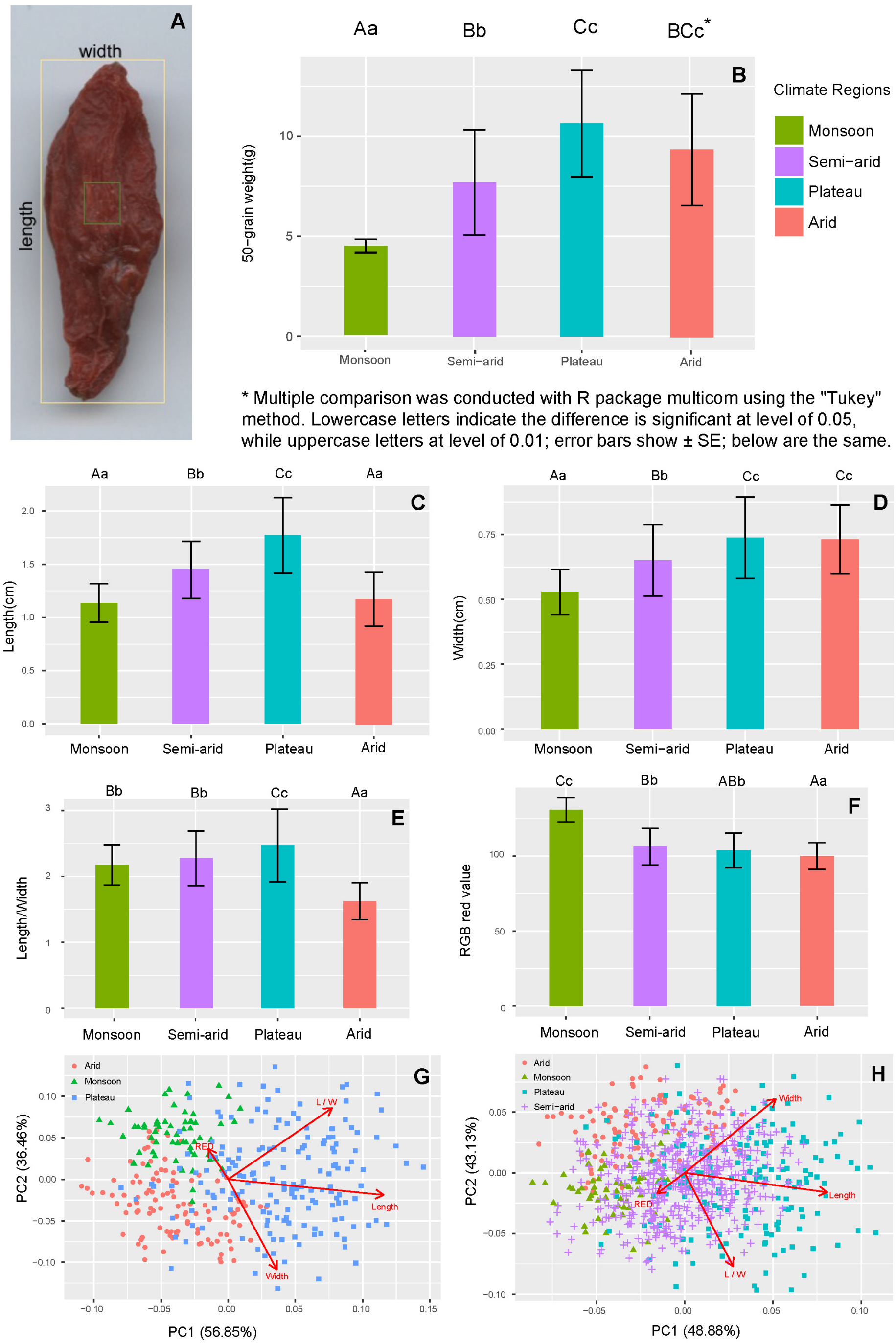

FIGURE 5 | Comparison of morphological traits of goji from different climatic regions. **(A)** Example of measuring shape and color; **(B)** Average weight per 50 fruits; **(C)** Average fruit length; **(D)** Average fruit width; **(E)** Average length/width ratio of fruits; **(F)** Average redness of fruits; **(G)** Morphological PCA score plot without semi-arid region; **(H)** Morphological PCA score plot of all regions.

spp. and *Curcuma* spp. can be separated successfully (Booker et al., 2014, 2016).

The typical spectra of goji from different climatic regions are shown in **Figure 6A**. Profile No.2 differs from the others in peak shape, especially between 2.50 and 5.00 ppm. PCA analysis with data from 0.00 to 10.00 ppm shows that the two species *L. barbarum* and *L. chinense* are separated by their metabolomics (**Figure 6B**). The region between 3.00 and 6.00 ppm, which importantly includes the signals from diverse sugars, turned out to differ strongly between the two species, which again becomes visible with PCA (**Figure 6C**); therefore, this part is a characteristic region for species identification.

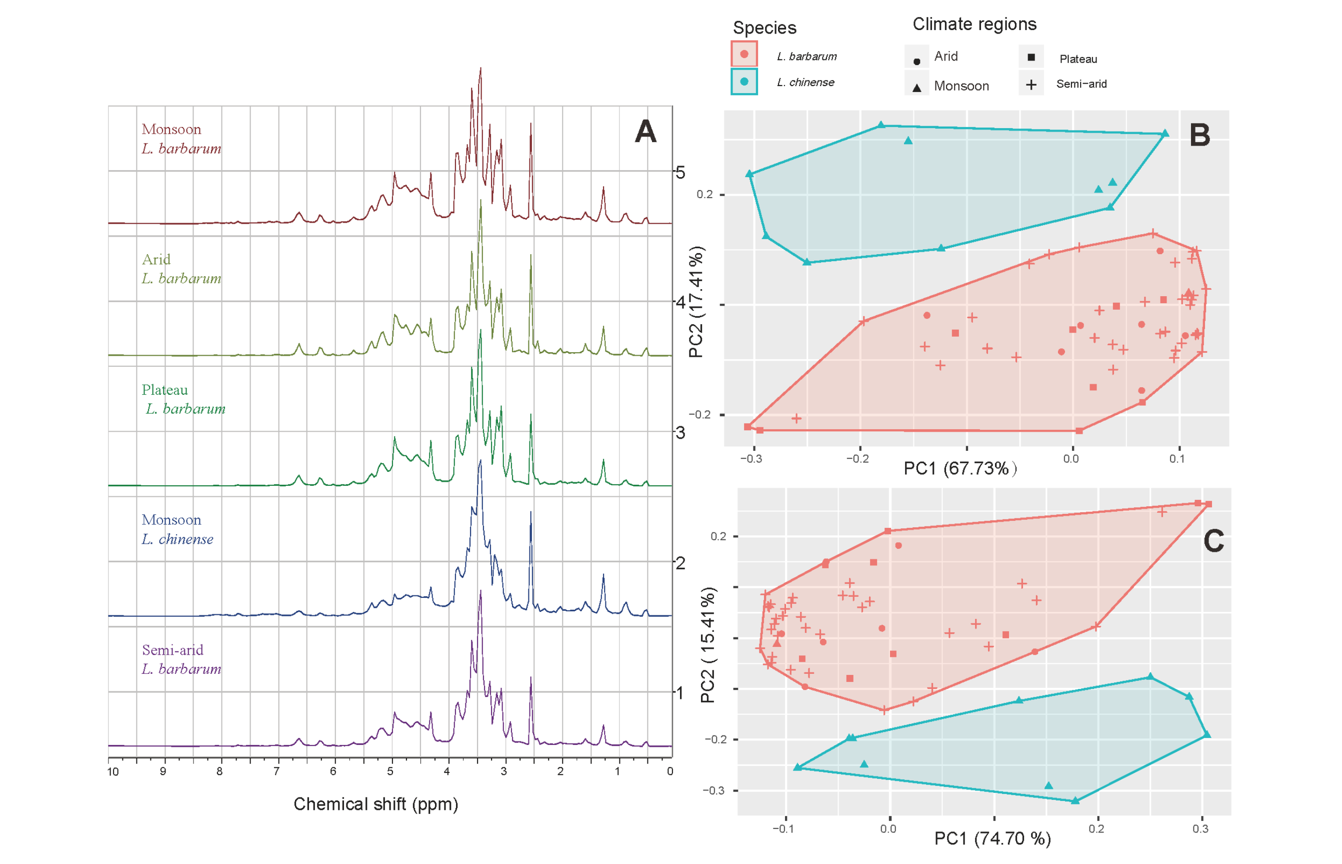

FIGURE 6 | [1]H NMR spectra and PCA projections of the first two principle components. **(A)** Spectra of goji samples from different climatic regions (δ = 10.00 – 0.00); **(B)** Score plot based on δ = 10.00 – 0.00; **(C)** Score plot based on δ = 6.00 – 3.00.

Similar results were reported with a chemometric approach based on Fourier-transform infrared spectroscopy (FT-IR), by which goji from Hebei was discriminated from that of other regions, while others were clustered closely (Shen et al., 2016). HPLC was successfully used to differentiate between genotypes of hybrid cultivars between *L. barbarum* and *L. chinense*, as well as fruit samples of the same genotype but dried in different methods (Donno et al., 2016b). Furthermore, chemometric approach was applied to FT-IR, high performance size-exclusion chromatography (HPSEC), and pre-column derivatization high-performance liquid chromatography (PCD-HPLC), which indicated that polysaccharides of goji from different regions barely differed (Liu W. et al., 2015). These findings are supported by a recent research which shows that the molecular structure of polysaccharides from goji (*L. barbarum* only) of different regions is highly similar (Wu et al., 2015). This similarity is also shown by our metabolomic analysis, where *L. barbarum* samples from different cultivation areas cluster together, but differ from *L. chinense*.

Hydrolyzed Sugar and Polysaccharides

Lycium chinense as well as samples from the semi-arid regions have significantly ($p < 0.01$) lower sugar contents compared to the plateau and arid region (**Figure 7A**). No differences in polysaccharide content could be found neither between the species nor the cultivation regions (**Figure 7B**).

Goji contains sugars at a relatively high level, and goji polysaccharides are recognized as main bioactive compounds (Xie et al., 2016; Yao et al., 2018b); as a result, sweetness and contents of polysaccharides are quality criteria of goji. The accumulation of sugar and polysaccharides in goji was reported to be affected by temperature, humidity, and altitude; variation even in the same climatic region is huge (Lei et al., 2013; Qi et al., 2016). Therefore, the differences among climatic regions are relatively small.

Analysis of the Antioxidant Activity

While all the IC_{50} values are far higher than that of the positive control, we find differences among goji from different regions. *Lycium chinense* from the monsoon region shows the highest antioxidant activity for all preparations, while goji from the plateau shows for most preparations the lowest antioxidant activity, although differences are non-significant ($p > 0.05$) (**Table 2**). Thus, *L. chinense* seems to be more potent as a natural antioxidant.

As traditional food supplement, goji has been used as medicinal liquor, i.e., soaked in spirit (40–70% EtOH),

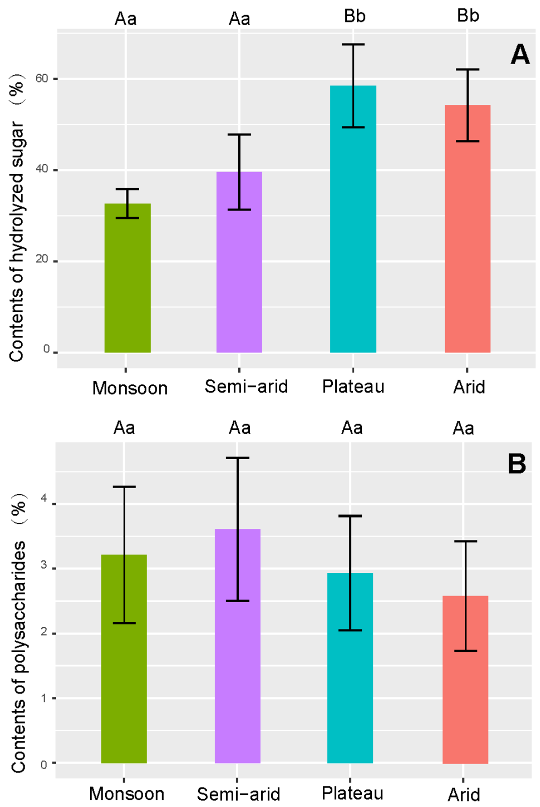

FIGURE 7 | Comparison of sugar content in goji from different climatic regions. **(A)** Average contents of hydrolyzed sugar; **(B)** Average contents of polysaccharides.

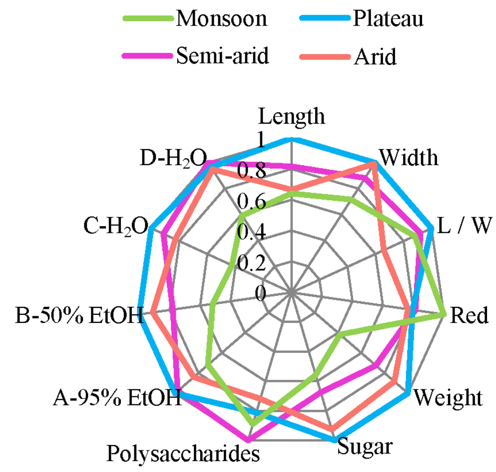

FIGURE 8 | Morphological, chemical, and antioxidant characteristics of goji from different climatic regions. Values are calculated by the ratio relative to the maxims.

as condiment boiled with food, or as tea infused with boiling water. Our extracts imitate these traditional uses (**Table 3**).

The highest antioxidant activity was found for the 50% EtOH extract which imitates medicinal liquor, followed by water extracts. The 95% EtOH extract shows the lowest activity. Our results therefore suggest that traditional goji wine acts as an antioxidant drink, as does goji tea, and do support the recommendation of goji as a natural antioxidant (Donno et al., 2015; Benchennouf et al., 2017).

Overall Comparison of the Different Regions and Species

Figure 8 summarizes the above morphological, chemical, and antioxidant data and provides a visual overview of similarities and differences. Overall, *L. chinense* from the monsoon region

TABLE 2 | IC_{50} value (µg/ml) for scavenging ABTS·$^+$ compared by regions*.

Climate	A-95% EtOH	B-50% EtOH	C-H_2O	D-H_2O
Arid	90.95 ± 2.45 ab	66.00 ± 3.30 ab	76.60 ± 3.10 b	70.65 ± 6.40 ab
Monsoon	77.90 ± 3.27 a	37.50 ± 0.16 a	39.30 ± 0.49 a	44.10 ± 1.80 a
Plateau	108.30 ± 5.40 ab	72.50 ± 3.70 b	92.55 ± 3.55 b	71.85 ± 7.75 ab
Semi-arid	105.74 ± 14.91 b	56.41 ± 13.42 ab	84.59 ± 13.09 b	74.51 ± 14.73 b

**The IC_{50} value of quercetin (positive control) was 0.75 ± 0.01 µg/ml (mean ± SE). Multiple comparison was carried out with the method of "Tukey"; and in the same column, means sharing the same letters are not significantly different from each other ($p > 0.05$).*

TABLE 3 | IC_{50} value (µg/ ml) for scavenging ABTS·$^+$ compared by preparations*.

Preparations	Monsoon	Semi-arid	Plateau	Arid
A-95% EtOH	77.90 ± 3.27 c	105.74 ± 14.91 c	108.30 ± 5.40 b	90.95 ± 2.45 b
B-50% EtOH	37.50 ± 0.16 a	56.41 ± 13.42 a	72.50 ± 3.70 a	66.00 ± 3.30 a
C-H_2O	39.30 ± 0.49 ab	84.59 ± 13.09 b	92.55 ± 3.55 ab	76.60 ± 3.10 ab
D-H_2O	44.10 ± 1.80 b	74.51 ± 14.73 ab	71.85 ± 7.75 a	70.65 ± 6.40 ab

**The IC_{50} value of quercetin (positive control) was 0.75 ± 0.01 µg/ml (mean ± SE). Multiple comparison was carried out with the method of "Tukey"; and in the same column, means sharing the same letters are not significantly different from each other ($p > 0.05$).*

(blue) differs most while the other regions are more similar, differing among few sensory characteristics only, such as length, weight and sugar contents.

CONCLUSION

Ningxia, with a semi-arid climate, always had the reputation of producing best goji quality (a so-called *daodi* production area). But today, new cultivation areas in different climatic regions are recognized as sources of good goji quality too. Depending on the criteria we look at, we find different patterns for goji quality in relation to area of production: Since the Tang Dynasty, goji from semi-arid regions was recognized for its superior quality; however, based on morphological and metabolomic characteristics as well as antioxidative activity it is not possible to separate semi-arid goji from samples from other regions.

Our results do not justify superiority of a specific production area over other areas. Rather, they suggest using goji from different regions for different purposes, based on the specific morphological and chemical traits. For example, large fruits from the plateau are suitable to be marketed as fresh fruits; goji with high sugar content is useful for conserved food; and high antioxidative activity combined with bitterness may suggest medicinal use.

The metabolomic approach combined with morphological analysis and bioactivity evaluation allows for capturing these different goji quality clusters, but, at the same time allows detecting outliers such as different species. This would not be possible with exclusive chemical analysis.

Fruits of *L. barbarum* and *L. chinense* differ in their metabolite profiles including HPTLC flavonoid fingerprint and ^{1}H NMR based chemometric analysis, as well as their antioxidant activity. As these two species are used interchangeably as medicinal goji, we suggest treating them as two separate botanical drugs. In case of food use, high sugar content and large fruit size are important, which supports the wider use of *L. barbarum* for food.

Future research on the bioactivity of the two species as well as samples from different cultivation areas beyond China will provide necessary data for specific and most appropriate uses.

AUTHOR CONTRIBUTIONS

RY, CW, MH, and YZ developed the concept for the study. RY drafted the paper. CW and MH supervised the study. Plant materials were collected by RY and YC. Morphological traits were measured by XZ and RY. HPTLC was supervised by ER and analyzed by RY. ^{1}H NMR was analyzed by RY at MH's lab and under his supervision. Contents of sugar was measured by RY and YC. Antioxidant activity was measured by YZ and YC. Data were analyzed by RY, YZ, ER, XZ, and YC. All authors revised the paper.

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Conflict of Interest Statement: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

CHAPTER 3

Quality control of goji (fruits of *Lycium* spp.): A value chain analysis perspective

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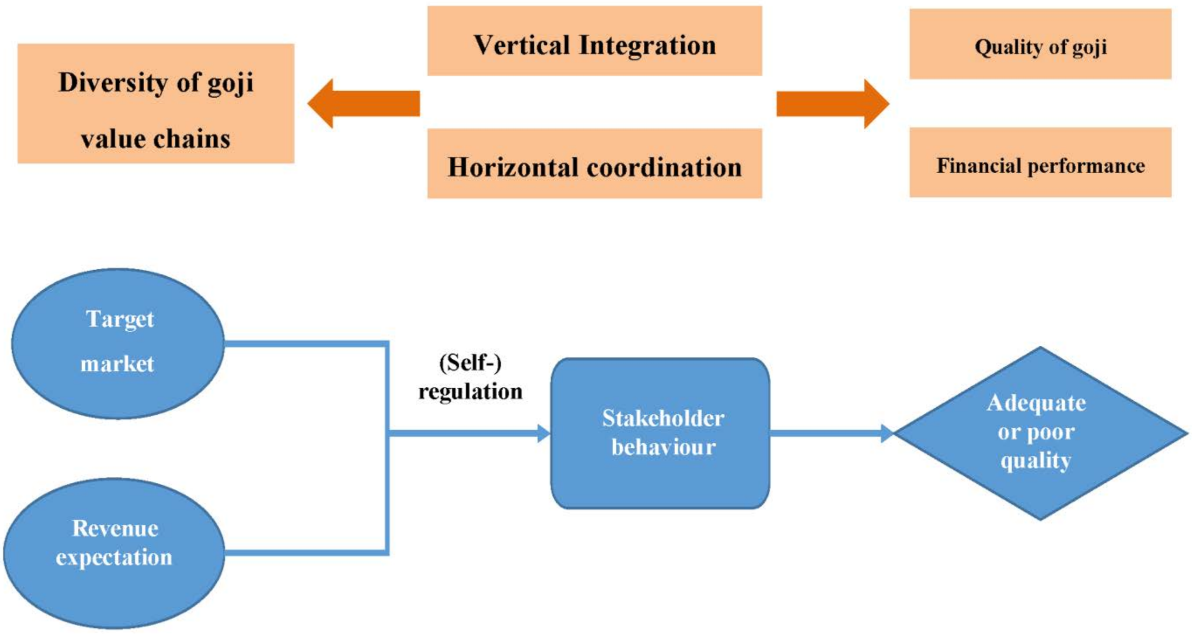

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Quality control of goji (fruits of *Lycium* spp.): A value chain analysis perspective

ABSTRACT

Ethnopharmacological relevance: Goji (fruits of *Lycium* spp.), which has been used as traditional food and medicine for thousands of years in Asian countries, is increasingly consumed globally as an herbal medicine. Quality of herbal medicines is critical for safe use and has been shown to be affected by value chains.

Aim of the study: Using a value chain (VC) framework, we aim at understanding the influence of different VC types on goji quality and revenue of stakeholders.

Materials and Methods: Participant observation and semi-structured interviews were conducted during five months of fieldwork in the main production areas in China with a total of 65 stakeholders. Quality of goji, behaviour and financial performance of stakeholders was documented and analysed for different VCs.

Results: Ten different types of VCs were identified. VCs with vertical integration and horizontal collaboration were found to have a more coherent quality control and better goji quality as well as improved stakeholders' financial performance. Vertical integration at different levels was found for independent farmer-based VCs, horizontal collaboration was found in the cooperative-based VCs. Full vertically integrated VCs were found in large-scale production.

Conclusions: Goji quality and stakeholders' revenues are linked with different types of VCs which mirror stakeholders' behaviour driven by target markets. Considering their positive influence on quality and revenues, well-developed vertically integrated value chains are likely to become more important in the near future.

Keywords: *Lycium*, goji, value chain, financial performance, stakeholders, quality control, traceability, herbal medicine product

1. Introduction

Humans rely on plants for food and medicine (Ekor, 2014; Gu and Pei, 2017; Heinrich, 2010; Knoss and Chinou, 2012; Leonti and Casu, 2013; Liu and Cheng, 2012; Qu et al., 2014). In the wake of globalization, traditional and local plant-derived foods are frequently turned into commodities such as food supplements or nutraceuticals. It is estimated that this is a market of over $ 150 billion with an annual increase rate of more than ten percent (Dillard and German, 2000; Hilton, 2017; Jennings et al., 2015; Shikov et al., 2017). Overall, traditional plant-derived foods and medicines are of increasing importance both, for health problems in people's daily lives and within the context of fast developing business networks and opportunities. However, the larger the market becomes the more quality problems arise (Posadzki et al., 2013). Most herbal medicinal products are applied in the form of mixtures which consist of hundreds of compounds, which makes quality control notoriously difficult (ChP Commission, 2015; BP Commision, 2017; EDQMH, 2017).

Moreover, in many countries the regulations of such classic formulas continue to be loose (Cyranoski, 2017; Qiu, 2007). Regulations for botanical food supplements are generally less strict and good quality is even more of an issue (Shao, 2017). Quality control of plant-derived products is crucial for their safety and effectiveness. However, are the present methods sufficient and what needs to be understood about the processes from the initial agricultural production / collection to the final commercial products?

Many quality control methods have been developed for the authenticity, purity, and the analysis of active substances of botanical products. They mainly rely on morphology, phytochemical analysis, and molecular identification. The most common methods are chromatography-based quantitative and qualitative analysis of constituents. These include high performance liquid chromatography (HPLC), thin layer chromatography (TLC) or high performance thin layer chromatography (HPTLC), infrared spectrometry (IR), gas chromatography (GC) and capillary electrophoresis (CE). Mass spectrometry (MS) is often used to identify substances and chemometrics is applied to analyse relationships among samples (Donno et al., 2016; Guo et al., 2017; Kokotkiewicz et al., 2017; Liang et al., 2004; Maldini et al., 2016; Martinez-Frances et al., 2017; Reich et al., 2006; Wagner et al., 2011). Molecular identification, including DNA barcoding and DNA metabarcoding, are seen as important tools for species authentication (Chen et al., 2010; Heinrich and Anagnostou, 2017; Jia et al., 2017; Raclariu et al., 2017; Xin et al., 2013; Zhang et al., 2001). Bioactivities are also measured and often applied together with metabolomic analyses (Donno et al., 2015; Liu et al., 2017; Walch et al., 2011). Considering the complexity of botanical products, profiles of active substances provide only limited chemical information with metabolomic approaches being better suited to depict this complexity. They were successfully used in quality control of botanical products such as coffee, camellia oil, goji, or *Rhodiola* species (Booker et al., 2016; de Moura Ribeiro et al., 2017; Heinrich, 2008; Kim et al., 2010; Pelkonen et al., 2012; Shi et al., 2018; Yao et al., 2018).

Safety is an important attribute of good quality. While safety issues may arise due to inherent toxic constituents of a plant, they usually are due to external contamination through, e.g., heavy metals, pesticides, microbes, mycotoxins, and sulphites. Fortunately, all these substances are detectable with suitable technologies (Fu et al., 2017; Kan et al., 2011; Posadzki et al., 2013; Rather et al., 2017; Sharma et al., 2017; Silins et al., 2014; Yang et al., 2018; Yang et al., 2017; Yu et al., 2017; Zhang et al., 2012). Accordingly, the current technologies allow for the evaluation of the metabolomic and biological properties, as well as the harmful ingredients of a botanical product. However, are these sufficient for ensuring the quality and safety of botanical products?

The concept of value chains, which provides a framework for describing links between producers and consumers focusing most notably on the socioeconomic benefits to producers (Booker et al., 2012) has in recent years been expanded to also include a basis for understanding the products' composition and thus their potential therapeutic benefits. Heinrich (2015) and Raclariu et al. (2017) mapped different quality control methods along production stages (source, manufacture, and retail), indicating that quality control is dynamic and may consist of various inspections along the supply chain of herbal products. Such measures were also applied onto functional foods, neutraceuticals, spices and herbs (Sarkisyan et al., 2017; Shao, 2017; Székács et al., 2018). Obviously, an effective quality control of a botanical product consists of a systematic control of the whole supply chain or value chain.

Value chain analysis has originally been used to expound the value-adding activities of an organization, including the primary activities and support activities (Porter, 2008; Porter, 2001). The term supply chain has been used for all movements from the raw material to the final product across different parties, and thus comprises exhaustive flows of materials, funds, and information (Mentzer et al., 2001). Commonly, the two terms are used synonymously and value chain refers to the life cycle of a product, from raw materials to final products (Ayers, 2010; Booker et al., 2012; Heinrich, 2015). A botanical product always transits several levels of stakeholders and organizations from cultivation to processing and distribution, before it reaches the final consumers (Székács et al., 2018).

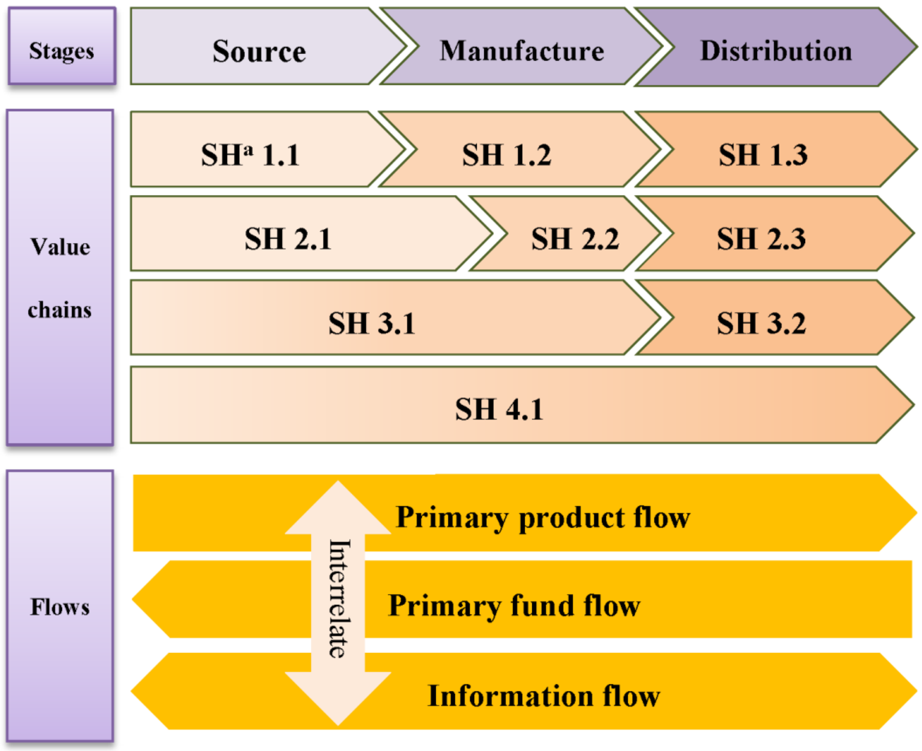

Fig. 1. Model of value chains and flow of materials in a value chain. [a] SH, stakeholder; adapted from Lambert et al. (1998); Raclariu et al. (2017); Székács et al.

(2018).

Value chains of the same product can be diverse. As is shown in **Fig. 1**, a value chain may include different stakeholders, who contribute at different supply stages. It has been argued that vertically integrated value chain (VIVC) generally result in a better quality of products and can also enable a fair compensation of producers (Aung and Chang, 2014; Booker 2016; Datta, 2017). In a supply chain, three main flows are distinguished: 1) information flow is bidirectional among stakeholders; 2) primary product flow is unidirectional from primary producer to consumer; and 3) primary fund flow is unidirectional from consumer to primary producer. These flows interact and influence each other as has been shown in many case studies (Booker et al., 2016; Howieson et al., 2016; Székács et al., 2018). In the case of turmeric, for example, the producers' livelihoods were found to vary among value chains. Integrated value chains were found to result in higher quality products, which were shown to have an impact on chemical variability and quality of the product (Booker et al., 2014; Booker et al., 2016). To understand the influence of different value chains of botanical products on both, the quality of the product and the income of the stakeholders, the three flows (product, information, and money) and their interrelatedness need to be analysed and understood.

In this study we analyse value chains of goji and their influence on stakeholders' financial performance as well as on the quality and safety of goji. In Asian countries the dried fruits of *Lycium* spp., namely goji or wolfberry, is a traditional medicine and food, and has become increasingly popular as a healthy food globally (Qian et al., 2017; Yao et al., 2018). China is the main production country and yields ca. 25 to 30 tons of dried goji annually (Cao and Wu, 2015; Xu, 2014). However, goji products are often of concern due to serious quality problems. For example, according to the US import alerts and EU RASFF notifications from 2009 to 2017, 208 batches of goji products were contaminated with pesticides or sulphur, of which some were even labelled as organic (FDA, 2017; RASFF, 2017). During our fieldwork in Chinese production areas in different climatic regions, we found diverse value chains interrelated to varying degrees with poor quality of goji, unfair sharing of revenues, and poor livelihoods of primary producers. Therefore the objectives of this research are:

What value chains exist for goji products? What information can be gained from a value chain analysis with regards to both best practices in supplying high quality materials and for identifying problems along the diverse value chains? What revenues gain the stakeholders in different value chains? How do finances and quality control interrelate? What are effective approaches for quality control and a fair sharing of revenues?

2. Materials and methods

2.1. Fieldwork

Goji harvesting time stretches from June to October. Fieldwork was done during five months of harvesting periods 2014, 2015 and 2016 in Zhongning County of Ningxia, Ge'ermu City of Qinghai, Jinghe County of Xinjiang, and Julu County of Hebei, which are the main goji production areas and trading centres in China (**Fig. 2**). Participant observation and semi-structured interviews were conducted with experienced participants of the goji industry: 24 farmers, 7 harvesters, 5 village leaders, 5 processing firm leaders, 14 retailers, 8 middlemen, directors of two official goji management institutions (Goji Management Bureau of Jinghe in Xinjiang and the Ningxia Goji Institute). Farmers, harvesters, village leaders, and retailers were selected randomly in the core cultivation areas or trading centre of the regions visited; middlemen were visited as follows: the first middleman was introduced by our counterpart in Ningxia, and the others were introduced by the first middleman; the interviewed institutions were introduced by our counterpart in Ningxia. Questionnaires for different participants are shown in **S2**; in addition, we encouraged the interviewees to provide any information as they wanted. Interviews were recorded with a voice recorder and stored in the first author's home. Moreover, two authors attended a national goji industrial summit which was held in Ningxia on 20th August, 2015.

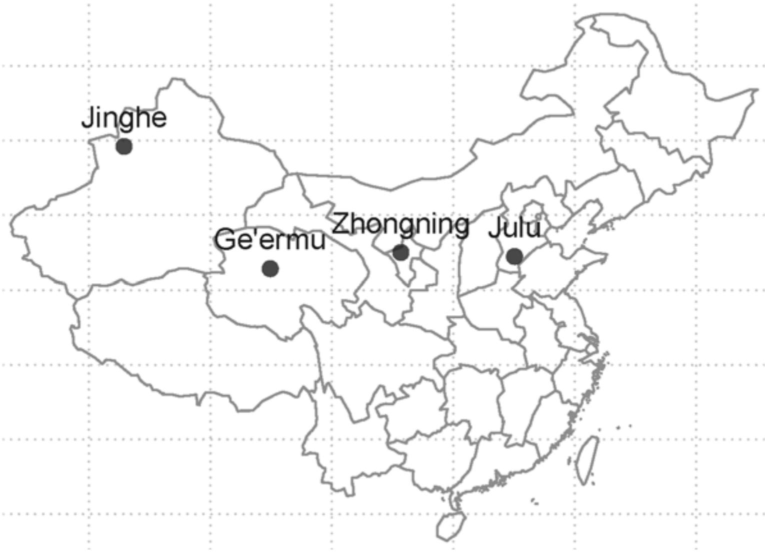

Fig. 2 Fieldwork sites in China. (Produced by R 3.4.3 with packages "maps" and "mapdata" (Brownrigg, 2016; Brownrigg et al., 2017; R Core Team, 2017))

2.2. Plant material

Fruits of *L. barbarum* and *L. chinense* were collected during fieldwork in China; samples were collected directly from the farmers, or offered by the institutions visited, or bought in Zhongning Goji Distribution Center, Julu Goji Yinhua Market, Xinjiang Jinghe Goji Market, Chengdu Hehuachi Chinese Herbal Medicine Market, and An'guo Chinese Herbal Medicine Market. Exported goji samples were bought in Switzerland, the UK, Germany, Poland, and Ireland. An authenticated reference standard sample of *L. barbarum* fruit was bought from the National Institute of Food and Drug Control of China, batch No. 121072-201410. Moreover, fruits with voucher specimens were collected in the National *Lycium* Germplasm Bank in Ningxia, Zhongning County of Ningxia, and Julu County of Hebei in July of 2016. Vouchers are deposited in the herbaria of the University of Zürich and ETH Zürich (Z+ZT). All samples are listed in **Table 1**.

Table 1 Sample information

Sample	Origin	Species	Stakeholder	Quality grade	Price* (Yuan/kg)
Q1	Qinghai	*Lycium*	Independent farmer	Rough	40~60

		barbarum L. (LB)			
Q2	Qinghai	LB	Independent farmer	Rough	40~60
Q3	Qinghai	LB	Independent farmer	Rough	40~60
Q4	Qinghai	LB	Independent farmer	Rough	40~60
Q5	Qinghai	LB	Independent farmer	Rough	40~60
Q6	Qinghai	LB	Independent farmer	Rough	40~60
Q7	Qinghai	LB	Independent farmer	Rough	40~60
Q8	Qinghai	LB	Independent farmer	Rough	40~60
Q9	Qinghai	LB	Independent farmer	Rough	40~60
G1	Gansu	LB	Independent farmer	Rough	40~60
G2	Gansu	LB	Independent farmer	Rough	40~60
G3	Gansu	LB	Independent farmer	Rough	40~60
G4	Gansu	LB	Independent farmer	Rough	40~60
M1	Inner Mongolia	LB	Independent farmer	Rough	40~60
M2	Inner Mongolia	LB	Independent farmer	Rough	40~60
M3	Inner Mongolia	LB	Middleman	Rough	70
M4	Inner Mongolia	LB	Middleman	Rough	65
X1	Xinjiang	LB	Retailer	Conventional	70
X2	Xinjiang	LB	Retailer	Conventional	80
X3	Xinjiang	LB	Retailer	Rough	70
X4	Xinjiang	LB	Retailer	Conventional	70
X5	Xinjiang	LB	Retailer	Conventional	100
X6	Xinjiang	LB	Retailer	Conventional	60
X7	Xinjiang	LB	Full-VIVC firm	Green food	100

N1	Ningxia	LB	Full-VIVC firm	Organic	130
N6	Ningxia	LB	Full-VIVC firm	Conventional	76
N7	Ningxia	LB	Full-VIVC firm	Conventional	70
N8	Ningxia	LB	Full-VIVC firm	Conventional	70
N9	Ningxia	LB	Independent farmer	Rough	60
N10	Ningxia	LB	Retailer	Conventional	50
N11	Ningxia	LB	Independent farmer	Rough	60
N12	Ningxia	LB	Independent farmer	Rough	40~60
N13	Ningxia	LB	Retailer	Conventional	76
N14	Ningxia	LB	Independent farmer	Rough	40~60
N15	Ningxia	LB	Independent farmer	Rough	40~60
N16	Ningxia	LB	Independent farmer	Rough	40~60
N17	Ningxia	LB	Independent farmer	Rough	40~60
N18	Ningxia	LB	Independent farmer	Rough	40~60
N19	Ningxia	LB	Full-VIVC firm	Organic	130
N20	Ningxia	LB	Full-VIVC firm	Conventional	70
N21	Ningxia	LB	Full-VIVC firm	Conventional	80
N22	Ningxia	LB	Full-VIVC firm	Conventional	70
E2	Germany	LB	Retailer	Conventional	289
E3	Switzerland	LB	Retailer	Conventional	632
E4	Switzerland	LB	Retailer	Organic	590
E5	Switzerland	LB	Retailer	Green food	489
E6	Switzerland	LB	Retailer	Conventional	312
E7	Switzerland	LB	Retailer	Organic	522
E8	Switzerland	LB	Retailer	Conventional	180
E9	Switzerland	LB	Retailer	GMP	459
E10	Switzerland	LB	Retailer	GMP, ISO 9001	459
E12	Switzerland	LB	Retailer	Organic	394

E13	UK	LB	Retailer	Conventional	186
E14	UK	LB	Retailer	Conventional	202
E15	UK	LB	Retailer	Conventional	174
E16	UK	LB	Retailer	Conventional	169
E17	UK	LB	Retailer	Conventional	227
E18	UK	LB	Retailer	Pharmacy	967
E19	UK	LB	Retailer	Pharmacy	967
E20	UK	LB	Retailer	Conventional	162
E21	UK	LB	Retailer	Organic	531
E22	UK	LB	Retailer	Pharmacy	677
E23	Ireland	LB	Retailer	Conventional	260
E24	Ireland	LB	Retailer	Conventional	288
E25	Ireland	LB	Retailer	Conventional	206
E26	Ireland	LB	Retailer	Conventional	231
E27	Switzerland	LB	Retailer	Conventional	426
E28	Poland	LB	Retailer	Organic	302
E29	Switzerland	LB, declared LC	Retailer	Organic	-
E30	Switzerland	LB	Retailer	Conventional	-
E31	Switzerland	LB	Retailer	Organic	-
H1	Hebei	LB	Independent farmer	Rough	25~50
H2	Hebei	*L. chinense* Mill. (LC)	Retailer	Conventional	180
H3	Hebei	LC	Retailer	Conventional	180
H4	Hebei	LC	Independent farmer	Rough	25~50
H5	Hebei	LC	Retailer	Conventional	60
H6	Hebei	LC	Retailer	Conventional	60
H7	Hebei	LC	Retailer	Conventional	180
H8	Hebei	LC	Retailer	Conventional	180

H9	Hebei	LC	Retailer	Conventional	180
H10	South Korea	LC	Retailer	Conventional	-
H11	Hebei	LB	Retailer	Conventional	60

2.3. Pesticides and sulphur residue measurement

High sensitive pesticide detector cards (Oasis Biochem batch number: 00120161911, China) were used to measure organophosphorus and carbamate pesticides. Added 2 drops of washing solution to a plain fruit surface, and then rubbed with another fruit; transferred 1 drop of the solution to the white side of the test card; waited for 10 min; and then folded the test card and kept at 38 ℃ for 3 min; and then checked whether the card was blue. After measurement the samples were categorized in three groups: frequent, seldom, or rare contamination.

SO_2 test tubes (Oasis Biochem, batch number: 20160425, China) were used to measure SO_2 residue. Soaked 0.5 g dried goji in 10.0 ml water for 10 min, and then transferred 1.0 ml of solution into a SO_2 test tube and shaked, and 3 min later compared the test tube to the colourimetric card. Control check was tested with pure water for each batch. Residues were presented as frequent, seldom, and rare according to the test results.

2.4. Value chain analysis

Firstly, procedures of goji production were compiled into an ordered flow sheet; secondly, stakeholders were added to corresponding procedures, so that stakeholders in the same chain were linked; thirdly, the labour cost and non-labour cost (mainly consists of materials, living costs, and outsourcing costs) of all stakeholders were calculated based on the interview data and cross-checked with information from goji industry, and then converted into Yuan/kg; fourthly, pesticides residue and sulphur residue of goji were linked with stakeholders. Finally, primary production behaviour was appended to corresponding stakeholders. The structure of value chains was mapped, and the financial performance, production behaviour, and quality of goji was analysed for each chain.

3. Results and discussion

3.1. Industrial structure and value chains

The earliest goji cultivation record was found in *Qianjin Yifang* published around C.E. 700 during the Tang Dynasty (Sun, 1998). Since the Ming Dynasty (around 1’300 C.E.), goji from Ningxia was listed in the tribute to the emperor, indicating that Ningxia yielded good quality goji (Cao and Wu, 2015). Since the 1960s, goji was introduced to Gansu, Xinjiang, Inner Mongolia, Qinghai, Tibet, and Hubei (Cao and Wu, 2015). Although Hebei was an independent historical production area with its unique germplasm, the superior cultivar from Ningxia was also introduced; therefore, commercial goji of two species were cultivated in Hebei. With a long production history, the goji industry formed several mature value chains. Although there have been many new products, dried fruits are still the main consumable.

Typically, goji goes through six stages before it reaches its consumer: 1) Cultivation, including activities such as ploughing, planting, pruning, irrigating, fertilizing, pest and disease controlling, and harvesting; 2) Preliminary processing, or roughing, applied on the fresh fruit, and including surface treatment and preliminary drying of fresh fruits (moisture is reduced to ca. 17%), as well as removing impurities; 3) Procurement, i.e. trading of rough goji produced in step 2; 4) Processing, including re-drying (moisture $\leq$ 13.0 %), removing impurities by winnowing, commercial grading, and packaging; 5) Wholesale, mainly to nonlocal markets; and 6) Retail. In each of these steps, different stakeholders can play a role, resulting in various forms of value chains (**Fig. 3**).

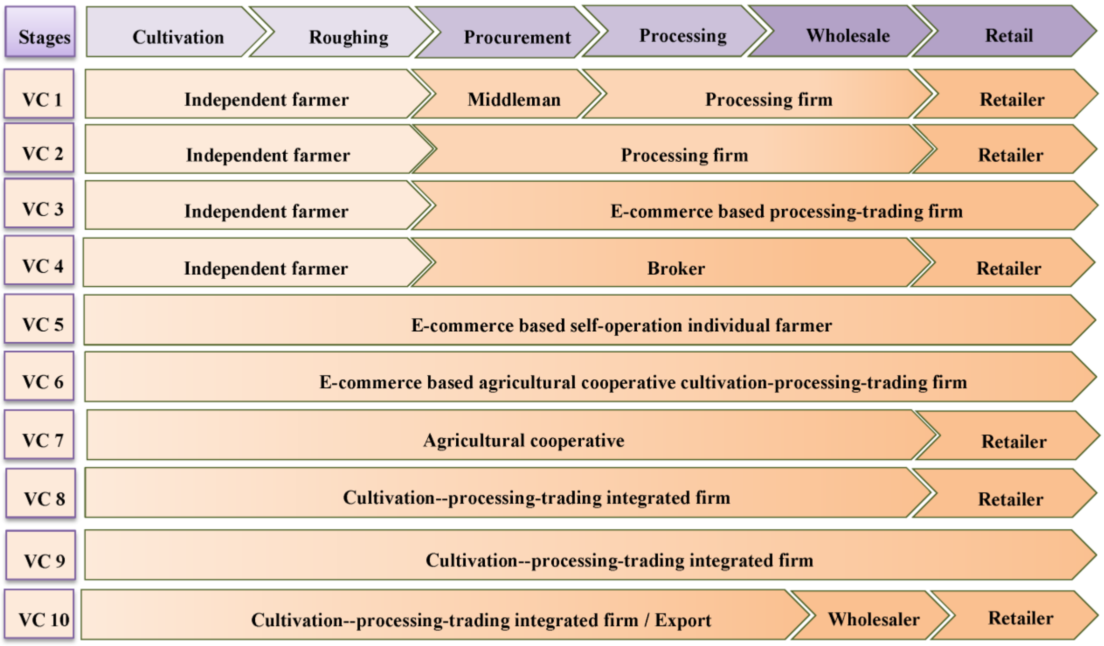

Fig. 3 Primary goji value chains (VCs) and the stakeholders involved. VCs 1, 2, 3, 4 are based on independent farmer; VCs 1, 2, 4, 7, 8 end with retailer; VCs 5, 6, and 9 are Full-VIVC; VC 10 is for exporting.

A key difference is found at the beginning of the VCs. 1) VCs 1 - 4 are based on independent farmers (with relatively small goji fields) offering their products to middlemen or other buyers; 2) VCs 5 is run by individual farmers (with small goji fields); 3) VCs 6 - 7 start with farmers involved in agricultural cooperatives (with relative large fields); 4) VCs 8 - 10 are charged by the cultivation-processing-trading integrated firms (with large-scale goji plantations). Among these four types of VCs, VCs 6 - 7 show horizontal cooperation. It is found that products of the same origin may flow into different VCs, which promotes the diversification of VCs.

Products of the ten VCs will finally reach their consumers by four channels, which consist of farmers, retailers, shops of full-vertically integrated value chains, and external retailers. VCs 1, 2, 4, 7, and 8 end with a retailer and this kind of merging increases the complexity of goji VCs. E-commerce is also important in goji trading. While E-commerce has been involved in VCs 3, 5, 6, it is increasingly accepted by retailers of other VCs as well.

Additionally, vertical integrations at different levels are found in goji VCs. Some stakeholders (e.g., processing firm) take over the roles of others, inducing vertical integrations. For example, VCs 2, 3, 7, 8 are partial-VIVCs, while VCs 5, 6, 9, which are controlled by single stakeholders, are full-VIVCs.

As traditional value chain, VC 1 has played an important role in the domestic goji market for decades. Independent farmers grow, harvest, and preliminarily process goji. Rough goji is sold via middlemen to processing firms; goji is further processed and bulk packaged and sold to retailers, who sell the product to the consumers. VC 1 is especially prevalent for goji cultivated outside Ningxia, such as from Gansu, Qinghai, and Inner Mongolia. In Qinghai, for example, independent farmers often have large goji fields, but the local firms are not sufficient for processing and local consumption is limited; therefore, middlemen sell the harvest to processing and trading centres in Ningxia. In average middlemen stay in Qinghai for five months every year, and are very important for this cross-province chain.

VC 2 and VC 3 are the results of the business expansion of processing firms. Due to the convenience of local trading centres, many processing firms are able to procure rough goji directly from the farmers. As the middleman's participation leads to price increase, this upstream expansion strategy results in direct economic benefits for the processing firms. Processing firms' direct procurement is not only found in local markets, but also in nearby production areas, for instance, firms in Ningxia may procure goji in Gansu. Additionally, the development of E-commerce makes it possible for a processing firm to expand downstream. Just like VC 3, the processing-trading firm is able to play the roles up to the retailer.

In VC 4, the brokers act as a bridge between farmers and nonlocal retailers. Contracts are made between the brokers and retailers: brokers procure rough goji, but outsource the processing, and finally send processed goji to the retailers; retailers will pay commission to the broker depending on the amount of goji.

VC 5 is a one-stop value chain conducted by self-operating individual farmers with relative large farms (ca. 1 to 2 hectares), who hire farm workers for production and processing. They sell their products via their own online shops. They may also sell their products to wholesalers.

VC 6 and VC 7 are agricultural cooperative-based value chains. Agricultural cooperatives are encouraged by the related governmental departments with beneficial policies. Farmers involved will get financial and technical support from the cooperatives, such as means of production, facilities for processing, and training in production technologies, and their products will be sold collectively, either to wholesalers, or consumers by online shops.

VC 8, VC 9, and VC10 are controlled by firms which control cultivation, processing and trading and are based on large-scale farms of over dozens of hectares. Their products are mainly sold to nonlocal retailers or consumers by their chain stores or online shops. In the case of the export chain VC 10, products are sold to foreign wholesalers who distribute to retailers such as supermarkets, groceries, and pharmacies.

3.2. Financial performance of stakeholders

Value of a product is created by the stakeholders' production activities. In different value chains, stakeholders always play different roles, and contribute different types of adding value by their labour inputs and non-labour inputs. **Table 2** shows the labour cost and non-labour cost along stages of the 10 main value chains.

Table 2 Labour cost (LC) and non-labour cost (NLC) of stages along goji value chains

Stage	Cultivation and roughing		Procurement		Processing and wholesale		Retail*	
Cost	LC	NLC	LC	NLC	LC	NLC	LC	NLC
VC 1	15.2 or 17.7	14.7 or 9.7	0.16	0.47	2.2	2	4.4 or 1.5	2 or 2.1
VC 2	15.2 or 17.7	14.7 or 9.7	0.16	0.47	2.2	2	4.4 or 1.5	2 or 2.1
VC 3	15.2 or 17.7	14.7 or 9.7	0.16	0.47	2.2	1.3	1.5	2.1
VC 4	15.2 or 17.7	14.7 or 9.7	0.65	0.1	0	4.8	4.4 or 1.5	2 or 2.1
VC 5	15.2 or 17.7	14.7 or 9.7	0	0	0	4.8	1.5	2.1
VC 6	15.2**	14.7	0	0	2.2	2	4.4 or 1.5	2 or 2.1

VC 7	15.2**	14.7	0	0	2.2	2	4.4 or 1.5	2 or 2.1
VC 8	15.2 or 20.8***	14.7 or 26.1	0	0	2.8	2.1	4.4 or 1.5	2 or 2.1
VC 9	15.2 or 20.8***	14.7 or 26.1	0	0	2.8	1.3	1.5	2.1
VC 10	20.8***	26.1	0	0	2.8	4.7	-	-

* For E-commerce, postage is borne by buyer; ** Policy: land rent free for 3 years; *** Policy: financial support for land rent and drying facility. Costs are presented as Yuan per kg of dried goji.

Most of the adding of value is achieved during the stage of cultivation and roughing. Non-labour cost at this stage consists of land cost, irrigation cost, fertilizer, and pesticides; labour cost includes work to care for the field, harvesting, and drying, and harvesting is the most costly part (ca. 45% of the whole costs), with an average of 13.5 Yuan (2.1 USD) / kg. However, the reward of people harvesting is not consistent with their labour input, and almost all of them are not satisfied with the working conditions. They need to pick fresh goji 15 hours per day, even during the hottest hours; with such intensive labour input, experienced harvesters can earn ca. 135 Yuan (21.3 USD) per day while the average wage is 90 Yuan (14.2 USD). Although harvesting machines exist; they are not widely applied though as they reduce labour input slightly but cause more impetus. For drying, farmers in VC 1 to 5 have alternative methods: i) drying in the sun, which needs more labour input but saves costs; ii) or drying in the artificial drying room by outsourcing to agencies, which costs less labour but processing charges of 5 Yuan/kg. As a traditional approach, the former is often practiced by independent farmers; considering their large amount, the latter is suitable for VC 6 to 10. Additionally, large-scale cultivation gains financial support from the government: for those with goji fields larger than 1.33 hectares, land use is for free during three years; also building of drying rooms can be done with the help of partial financial subsidies. For organic production chains, VC 8, 9, and 10, costs are higher because of by increased cost of labour and organic fertilizer, and the cost for certification and management. Cultivation and roughing add most value to goji, but independent farmers obtain small margins only because of the risk of price fluctuation and their low bargaining power.

Procurement is a key process in VCs 1 to 3 and is driven by middlemen. Their costs include procuring and reselling labour, travelling cost, and transportation cost. As a linkage of bulk trading among different geographical sites, middlemen need a rather high capital turnover, ranging from 0.6 to 1.5 million Yuan. As the turnovers are not always smooth, credit operations are important to them. For credits, non-governmental organizations such as goji chambers of commerce are founded, which provide financial guarantees to their members. However, in other chains, the function of middlemen are omitted or replaced, e.g. by brokers in VC 4. Compared to the cost of middlemen, those of brokers are higher in labour input and lower in non-labour input. This may be due to the smaller amount of goji processed by brokers per day (ca. 100~200 kg per day vs. ca. 1000 kg per day by middlemen), which increases the average cost of labour; brokers are working locally, which leads to low travelling costs.

Processing and wholesale are also labour-intensive stages, which include colour-based separation, re-drying, hand selecting, size-based grading, and transportation. The operational cost of the whole is 4.2 Yuan/ kg. In case of the direct selling chain (VC 3) the cost on transportation decreases; however, processing charge for outsourcing is 4.8 Yuan/ kg, as in VC 4 and VC 5; in the well-controlled chains (VC 8, 9, and 10), cost for quality control increase.

Retail, mainly run by high-street or shopping mall stores or online shops, is the final step to reach the consumer. Physical stores are traditional, which can be chained or independent, and the additional cost is made up of rent, labour and packaging. Due to its low start-up cost and operational cost, online shops become increasingly popular. There is no restriction to location, and to set up a new online shop, 10 000 Yuan (1580 USD) is enough, which is much cheaper compared to a small physical store (at least 60 000 Yuan (9480 USD)). According to our internet investigation, much more goji is sold by taobao.com compared to physical stores. For example, on November 11th, 2017, during the online shopping festival, about 179 tons of goji were sold in one hour. The monthly sales volume of a common physical shop is about 450 kg, which is lower than that of an online shop (ca. 4200 kg). Online shops are favoured both by retailers and consumers because of their low costs and shopping convenience. The export chain of organic goji, VC 10, has higher cost on quality control, customs clearance and international transportation. Outside of China goji is typically sold in health food shops, Asian markets and pharmacies, as well as online shops. According to **Table 1**, differences in the retail were found between the conventional goji and quality certified goji in domestic market, while the exported goji enjoys a much higher price.

The stakeholders will obtain profit by margin when they sell their products to the next stakeholder and the margin is impacted by the stakeholders' bargaining power and price fluctuation. As is summarized by Coff (1999), bargaining power is determined by the stakeholder's capacity of unified action, access to information, replacement cost, and exiting cost. Evaluated by these criteria, the large stakeholders have strong bargaining power. In VC 1 for example, independent farmers, especially those in rural areas, do not have reliable access to market information; while their rival, the middlemen, have direct contacts with the distribution centres; as a result, farmers are often disadvantaged. The price fluctuation of rough goji during the last five years (**Fig. 4**) also indicates the drawback of independent farmers.

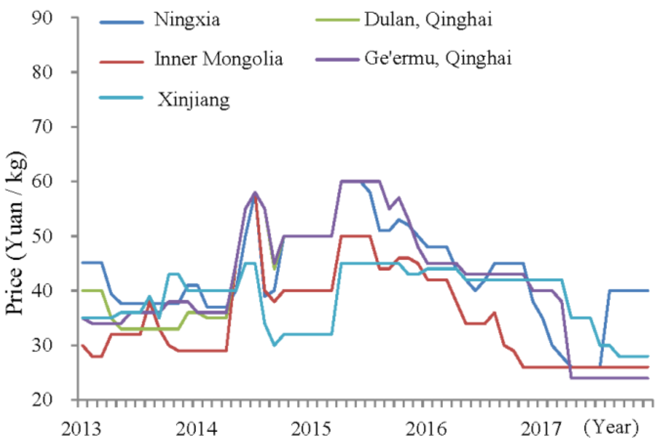

Fig. 4 Price fluctuation of rough goji in local markets from 2013 to 2017. The average monthly price data were extracted from http://www.zyctd.com/.

The price of rough goji ranges from 24 Yuan (3.8 USD) / kg to 60 Yuan (9.5 USD) / kg, and the coefficient of variation (CV) is between 14.26 % and 26.23%. The lowest cost is 27.4 Yuan (4.3 USD) /kg; thus, the price can be lower than the cost, which results in a deficit for the farmers. Although our interviewees may storage goji when the price is lower than they can accept, it is still a bet: the quality of goji will decrease during (prolonged) storage, and it is not certain that prices will rise soon. As a result, independent farmers in Ningxia started to turn goji into maize fields, which provides a more stable income. Alternatively, independent farmers are integrated in agricultural cooperatives, within which they obtain technological support, sale information, and stronger bargaining power. Large-scaled goji production is largely supported by governmental funding, such as reduced land rent and allowance for drying facilities. These economic conditions promote the larger scale production of goji in the upstream value chains, such as VCs 6 to 10.

The midstream (procurement, processing, and wholesale) which is traditionally charged by middlemen, processing firms, and trading firms may be prone to poor coordination of stakeholders. This results in the risk of discontinuity of material flow and financial return, which are vital for smallholders. For example, an overdue payment may lead to bankruptcy of a middleman. Thus, there is a trend towards horizontal coordination in the midstream, such as VCs 2 to 10.

Although procurement price fluctuates drastically, the retail stage enjoys a stable price, offering a stable market to the stakeholders who are close to the consumers. This may stimulate processing firms and agricultural cooperatives to extend downstream to open retail businesses (VCs 3, 6, 9), or may even lead to the rising of self-operation farms (VC 5).

3.3. Quality evaluation of goji along value chains

The quality criteria of goji are published in different types of documents, such as pharmacopoeias and industrial standards (esp. of the food industry). Fruit weight and sugar contents are commonly used indices, while the contaminants such as pesticides residue, sulphur residue and heavy metals are often controlled for safety reasons. However, when being asked “what is good quality goji?” our interviewees always referred to the morphological and sensory traits of goji but never safety issues. Therefore, a quality investigation of goji from different value chains was exerted and the results are shown in **Table 3**.

Table 3 Quality evaluation of goji and possibility of hazard risks along different value chains

Value chain	Traceability	Certify	Control	Pesticide residue	Sulphur residue	Possibility of hazard risks		
						Cultivation	Drying	Processing
VC 1	No	No	Weak	Frequent	Frequent	Likely	Possible	Improbable
VC 2	No	No	Weak	Frequent	Frequent	Likely	Possible	Improbable
VC 3	No	No	Weak	Frequent	Frequent	Likely	Possible	Improbable
VC 4	No	No	Weak	Frequent	Frequent	Likely	Possible	Improbable
VC 5	Yes	No	Weak	Frequent	Seldom	Possible	Improbable	Improbable
VC 6	Yes	Maybe	Medium	Seldom	Seldom	Possible	Improbable	Improbable
VC 7	Yes	Maybe	Medium	Seldom	Seldom	Possible	Improbable	Improbable
VC 8	Yes	Yes	Strong	Rare	Rare	Improbable	Improbable	Improbable
VC 9	Yes	Yes	Strong	Rare	Rare	Improbable	Improbable	Improbable
VC 10	Yes	Yes	Strong	Rare	Rare	Improbable	Improbable	Improbable

As an effective quality control tool complied with legislation in food industries, traceability was applied to improve the safety of food and the confidence of consumer, as well as to connect producers and consumers (Aung and Chang, 2014; Dabbene et al., 2014; Regattieri et al., 2007). However, goji of the value chains including independent farmers, viz. VC 1 to VC 4, have poor traceability. Since the independent farmers sell their goji in large quantities to other stakeholders, traceability becomes impossible. In other chains, where rough goji is directly processed, traceability is feasible. With the increase of consumers' concerns on traceability and the development of information technology, a traceability system for goji has been available to the public by Quick Response (QR) Code since 2015. This QR code has also been encouraged by the government, for example, Zhongning County offers an allowance of 0.03 Yuan / piece. Since bulk goji loses traceability at the auction, but policy and consumers are in favour of it, value chains VC 1 to VC 4 are inferior in this respect.

Certification of a product, such as organic food, increases consumer's confidence, especially in the health food market. Driven by the market, goji production is subject to certification. Perhaps the most attractive certification is the organic certification. However, in 2012 considering the complexity of goji production, Chinese Certification and Accreditation Administration (CNCA) discontinued organic certification of goji in China, and goji products in China were not permitted to be advertised as organic any longer. However, in order to meet the demands of foreign high quality markets, goji producers applied for certifications from organizations abroad, such as EU organic and HACCP (Hazard Analysis Critical Control Point). Practically, small stakeholders cannot afford these certifications. On the other hand, companies involved in VC 8 to 10, who deal with large amounts of products for high quality markets, are always certified. For agricultural cooperatives, certifications are always not certified.

Formal legally binding regulations or self-regulations are considered to be essential for good quality (Booker and Heinrich, 2016; Booker et al., 2015). However, without a powerful regulatory authority, and weak self-regulation, the processes of the individual stakeholders are generally not well-regulated. Conventional production relies on chemical pesticides and biocides for pest and disease control, and chemicals will be applied 8 to 10 times during an annual production cycle. Independent farmers tend to apply excessive amounts of chemicals, which leads to problematic residues. Furthermore, a few farmers paid little attention to the safety interval before harvesting. These undesirable conditions have been caused by: poor education on how to use chemicals properly, and, while recommendations from pesticide sellers exist, no powerful regulatory authority controls the use of these substances. Also, pesticide residue detection is costly and therefore largely lacking in the value chains VC1 to VC4. Compared to pesticides, sulphur is easier to detect and control, but overuse still exist in products from some value chains.

Safety hazards of goji samples are found to be linked to practices in cultivation, drying, and processing, and mainly existed in the independent farmers' value chains. During cultivation, goji is exposed to pesticides; when drying, goji may be exposed to pesticides again, as well as unhygienic conditions if dries by the road side; and while processing, low quality products may again be exposed to unhygienic conditions.

3.4. Relationship among behaviour, revenue, and quality

Goji is traditionally consumed as medicine and food. Nowadays, there is an increasing demand for high quality goji products. Therefore, goji products are involved in two types of markets: the conventional market and the high quality market. Since products for these two markets differ completely in their supply chain, their behaviour-economic-quality was analysed comparatively (**Fig. 5**).

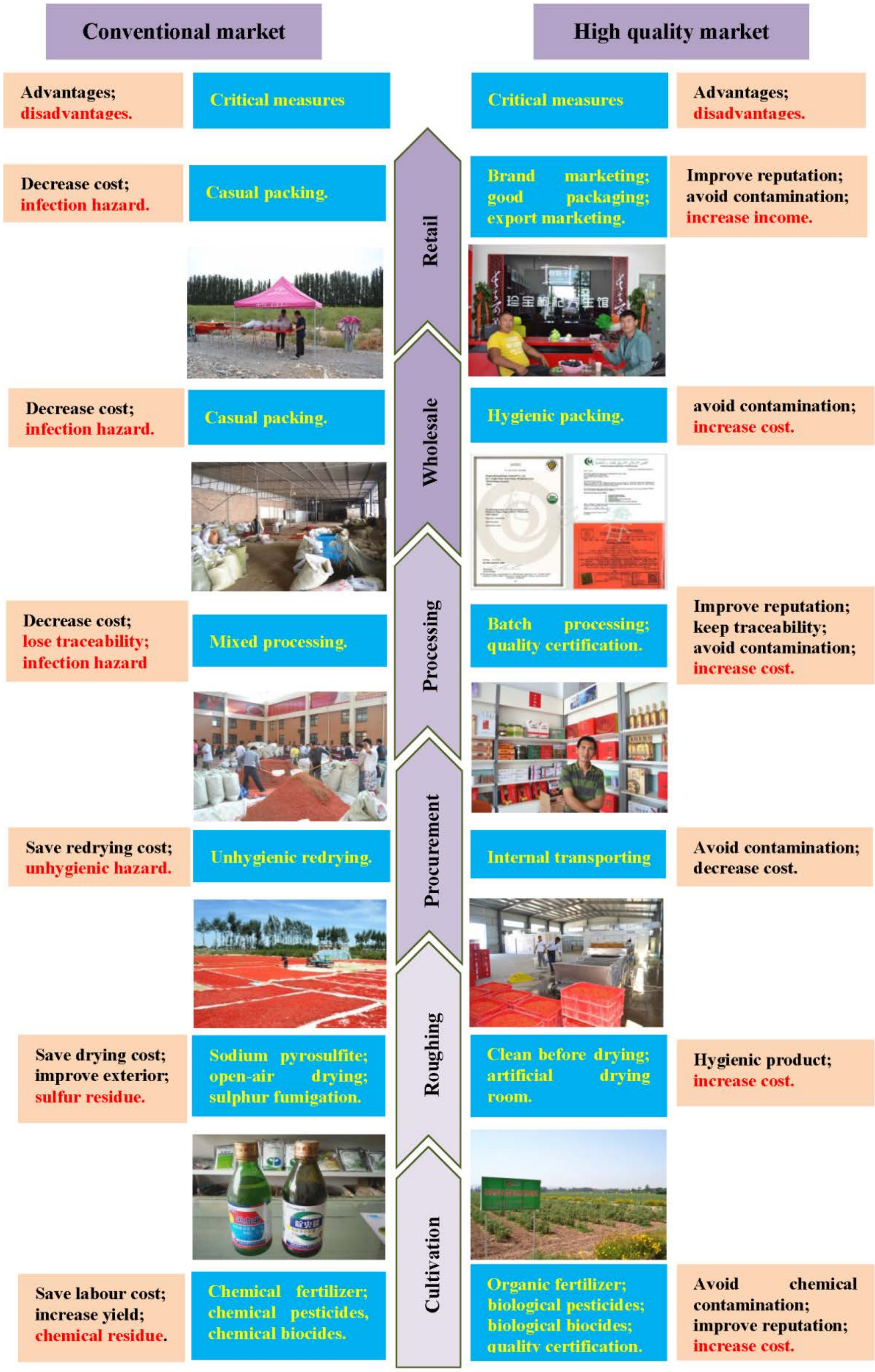

Fig. 5 Critical measures and their advantages/disadvantages along value chains of conventional market and high quality market (Based on Booker and Heinrich (2016))

Stakeholders in both types of value chains want to increase profit, however, with different measures: in conventional market oriented value chains measures are taken to decrease costs and increase yield which causes quality loss; while in the high quality oriented chain products' quality and firms' reputation are improved, which increases the overall costs. High quality goji producers would get higher revenues from the consumers, while stakeholders of the conventional market will get paid less. Therefore, the behaviour and revenue of stakeholders are linked with the quality and target market of products (**Fig. 6**).

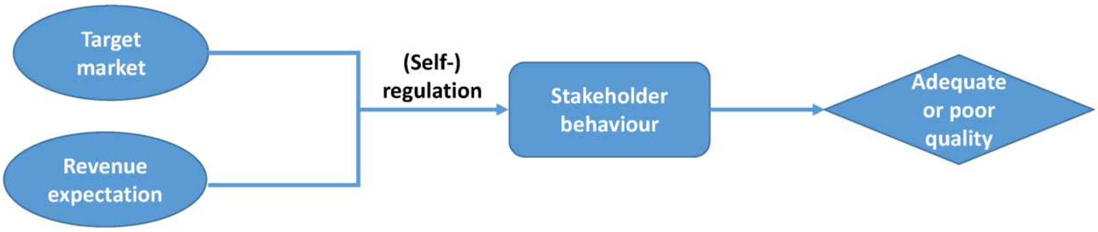

Fig. 6 The relationship among the target market, revenue expectation, behaviour, and quality

The intended target market has direct impact on stakeholders' revenue. According to our investigation, the price of goji in conventional market (40 ~ 60 Yuan (6.3 ~ 9.5 USD) /kg) is lower than that of the high quality market (such as green food and organic, 70 ~ 130 Yuan (11.0 ~20.5) /kg). The revenue expectation will induce the stakeholders' behaviour. Stakeholders for conventional market are inclined to reduce the production cost. Lower production cost results in behaviours which often pose quality risks, such as the application of pesticides. Consequently, the quality of goji is a direct consequence of the commercial decisions and the resulting production practices by the various stakeholders. Also, the quality of goji will further determine which market it could go. VCs 1 to 4 are examples of conventional market value chains. With the traditional target of getting high yields, chemicals and unhygienic measures are applied to goji without professional guidance, therefore, quality problems are common and these goji could enter the conventional market with relative lower revenue. Products of VCs 5 to 7 can enter both markets, although they may not have quality certifications. Their production behaviours are mainly self-regulated, and reputation is built by reliable production and traceability. Value chains VC 8 to VC 10 are for high quality markets, with the effective quality control during production and reliable quality certifications, these value chains produce goji of high quality, which brings high financial return to the stakeholders.

4. General discussion

In order to fulfil the increasing demand of the global market, the supply system of goji has recently undergone great changes, resulting in a diversity of value chains. Vertical integration, horizontal collaboration, outsourcing, and E-commerce are found to emerge in goji value chains at different levels.

Vertical integration is induced by the business expansion of stakeholders. VCs 2 and 3 are the result of vertical integrations of processing firms, by taking over procurement (forward integration) and retail (backward integration). Of all the ten value chains, VC 1 is without vertical integration, while VCs 2, 3, 4, 7, 8, 10 are partially integrated, and VCs 5, 6, 9 are full VIVCs. Vertical integration was reported to have many benefits, such as overcoming barriers among stakeholders, increasing financial profits, and decreasing price fluctuation (Görg and Kersting, 2014; Hanson, 2015; Shahidullah and Haque, 2010). These benefits are all found in goji value chains, especially in those full VIVCs (VCs 5, 6, 9). The full vertical integration value chain was thought to be a competitive approach, within which all the production stages were conducted by one stakeholder (Booker et al., 2016; Gereffi et al., 2005; Shahidullah and Haque, 2010). In the case of goji, farmers will get access to the market, as well as technological and financial support by joining vertically integrated value chains (Liu et al., 2015). Additionally, partial vertical integration attributes to a reliable traceability of its products.

Horizontal collaboration is shown as the alignment of stakeholders in charge of the same production stage, e.g. the agricultural cooperative. With a higher level of communication, trust, and common goals, agricultural cooperatives have higher revenue for the involved stakeholders, and chemicals used are better controlled (Martínez-Victoria et al., 2018; Wollni and Zeller, 2007; Zhou et al., 2018). In the value chains VC 6 and 7, farmers of agricultural cooperatives enjoy better economic status while the quality of goji is better controlled too. Therefore, for individual farmers to join agricultural cooperatives could be a strategy for improving the quality of goji and stakeholders' revenues in VCs 1 to 4. Also the chamber of commerce founded by the processing and trading firms is an example of horizontal integration.

Outsourcing is found in several chains such as VC 4 and 5. Expensive facilities, such as artificial drying rooms and grading machines, are not available for the smallholders, while the proprietors of these facilities are willing to obtain more profits, therefore, the outsourcing business raised. Despite its function of resource allocation, outsourcing can bring disadvantages including quality problems (Dinu, 2015; Lahiri, 2016). Due to the existence of smallholders, the outsourcing would continue.

E-commerce offers a convenient and inexpensive approach for retailers to build direct access to consumers. While goji is produced in distinct areas of China, retail of goji gets rid of spatial limitations. Since costs for running an online shop are low, they increase in number and are vertically integrated by processing firms.

5. Conclusions

With an insight into value chains of goji, our results indicate that goji's quality, stakeholders' behaviour and revenue are correlated. It is found that stakeholders' behaviour, which is driven by the target market, leads to quality differences, which further determine the financial return of stakeholders. Therefore, coordination of relationships in value chains could be a strategy for quality control of goji.

The diverse value chains are induced by vertical integrations and horizontal collaborations, while E-commerce promotes the vertical integration. Vertical integration and horizontal collaboration are beneficial to both quality of goji and revenue for stakeholders; therefore, the related value chains are increasingly developed. Since well-developed VIVCs supply products with good traceability, reliable quality, and ensure adequate financial revenues of the stakeholders involved, in the future they are likely to become more important.

Quality control of herbal medicine products relies on quality regulation frameworks and quality inspections. Our study shows that quality is impacted by production process and financial performance, indicating that a robust value chain is the core of quality control. With a value chain analysis including social-economic and quality factors, the present work emphasises the importance of the process control in herbal medicine products.

AUTHOR CONTRIBUTIONS

RY, CSW, and MH developed the concept for the study. RY and ZW drafted the paper. CSW and MH supervised the study. Fieldworks were conducted by RY with the critical help of ZW; plant materials were collected by RY and ZW; pesticides residue, and sulphur residue were measured by RY; ZW contributed critical financial data and behaviour information, and value chain analysis was carried out by RY and ZW. Data were analysed by RY and ZW. All authors revised the paper.

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SUMMARY

Despite its increasing popularity with the global healthy food market, goji is still some mysterious to the public: Where is it from? What benefits does it have? How is it produced? How to get goji of high quality? The present thesis employs an interdisciplinary ethnobotanical methods to answer these questions.

Firstly, by a botanical, ethnobotanical and historical review, the the food and medicine use of *Lycium* in the worldwide was revealed. In total, 35 of the 97 species were found to be used as food and/or medicine by peoples from different regions. Regarding to the traditional uses of *Lycium*, the used species, plant parts, and usages are found to be differ amongst cultures. The earliest medicinal use of *Lycium* was found in China (since ca. CE 100), and a series of time-continous historical herbals recorded the development of knowledge on *Lycium*. Recently, many phytochemical and pharmacological studies, mostly on goji (fruits of *L. barbarum* and *L. chinense*), explain the linkage between traditional uses and bioactive compounds; the diversity of plant usages offers opportunities for the development of new food and or medicine products, and it can be inferred that the phytochemical and pharmacological studies will be helpful to the development of other species and usages. It is found that the quality criteria for goji differ among regions according to a pharmacopoeia comparison, which may lead to obstacles in trading as an international consumption. Therefore, a relative uniform quality criterion is recommended. Such a transdisciplinary approach will serve as a model for studying traditional food or medicine plants.

Secondly, by a morphological, metabolomic, and antioxidant bioactive analysis, goji of different climatic regions in China was compared. Historically goji was recorded to be cultivated in monsoon region, and then the semi-arid was considered to yield the good quality goji since ca. 700 CE. Recently, Ningxia is thought to be the “daodi region” of goji, and is the centre for goji trading and research. However, our results do not justify superiority of a specific production area over other areas. Rather, they suggest using goji from different regions for different purposes, based on the specific morphological and chemical traits. The metabolomic approach combined with morphological analysis and bioactivity evaluation allows for capturing these different goji quality clusters, but, at the same time allows detecting outliers such as different species. This would not be possible with exclusive chemical analysis. Moreover, considering the obvious differences of metabolite profiles and antioxidant activity

between fruits of *L. barbarum* and *L. chinense*, we suggest treating them as two separate botanical drugs. Future research on the bioactivity of the two species as well as samples from different cultivation areas beyond China will provide necessary data for specific and most appropriate uses.

Thirdly, according to a value chain analysis on goji industry in China, ten value chains were idenfied, while the relationship amongst stakeholders' production behaviours, stakeholders' financial performances, and goji's quality was revealed. It is found that stakeholders' behaviour, which is driven by the target market, lead to the quality differences, which further determine the financial return of stakeholders. Therefore, coordination of relationships in value chains could be a strategy for quality control of goji. The diverse value chains are induced by vertical integrations and horizontal collaborations. Vertical integration and horizontal collaboration are beneficial to both quality of goji and revenue of stakeholders, therefore, the related value chains are increasingly important. While the well-developed VIVCs supply products with good traceability, reliable quality, and ensure adequate financial revenues of the stakeholders involved, they are excepted to become more important in the future. While quality is impacted by production process and financial performance, a robust value chain is the core of quality control. With a value chain analysis including social-economic and quality factors, the present work emphasises the importance of the process control in herbal medicine products.

Overall, this thesis present a systematic knowledge of goji covering the traditional and current uses, quality assessment, and value chain. In the meanwhile, it offers a template for understanding the ethnobotany and quality control of such botanical consumbles which are from traditional to global. Hopefully, this interdisciplinary ethnobotinical study framework would be a model for studies on those traditional food and medicine plants.

APPENDIX

S1 *Lycium* records in Chinese herbals of all dynasties[*]

Year	Herbal Title	Used parts	Usages	Notes	Reference[**]
Ca. C.E. 100	*神农本草经* *Shennong Bencao Jing*	Unclear	Treat evil qi, heat, *xiaoke*, and arthralgia; physical strengthen, anti-aging	Flavor bitter, temperature cold	Shang, 2008
Ca. 208-239	*吴普本草* *Wupu bencao*	Unclear	(not mentioned) NM	With 2 names: 杞芭 *qiba*,羊乳 *yangru*	Wu, 1987
Ca. 350	*抱朴子* *Baopuzi*	Unclear	Extend longevity	Only name mentioned	Ge, 1995
Ca. 350	*肘后备急方* *Zhouhou Beiji Fang*	Root, fruit	Anti-fatigue, deodorant and antiperspirant, mania of dog	Formulas included	Ge, 1999
Ca. 420-479	*雷公炮炙论* *Leigong Paozhi Lun*	Root, fruit	NM	Process method of root; fruit was used for processing the herb *巴戟天 bajitian*	Lei, 1985
Ca. 492-500	*本草经集注* *Bencaojing Jizhu*	Root, leaf, stem, fruit	Treat rheumatism, headache, evil qi, heat, *xiaoke*, arthralgia; physical strengthen, anti-aging; leaf porridge	Root, fruit were separate. Collecting times of root, leaf, fruit	Tao, 1994
Ca. 502-536	*名医别录* *Mingyi Bielu*	Root, leaf, stem, fruit	Rheumatism, headache, physical strengthen, anti-aging, enhance *yin*	Root, fruit were separate. Collecting times of root, leaf, fruit	Tao, 1986
659	*新修本草* *Xinxiu Bencao*	Root, fruit, leaf	Treat rheumatism, headache, evil qi, heat, *xiaoke*, arthralgia; physical strengthen, anti-aging; leaf porridge	Root, fruit were separate; collecting times of root, leaf, fruit	Su, 1981
682	*千金翼方* *Qianjin Yifang*	Fruit, leaf, root,	Treat evil qi, heat, *xiaoke*, and arthralgia, eye, calculus, spasm; food use, physical strengthen, anti-fatigue, tooth regeneration, enhance *yin*	Harvesting, cultivation were included; different parts were used solely or in formulas	Sun, 1998
Ca. 618-907	*食疗本草* *Shiliao Bencao*	Fruit, root, leaf	Treat rheumatism, headache, evil qi, heat, *xiaoke*, arthralgia, eye problem; physical strengthen, nourish, leaf tea enhance male's sexual performance	Recipes of medicated diet, leaf juice was used on eye	Meng, 1984
1062	*本草图经* *Bencao Tujing*	Leaf, fruit, root	Treat rheumatism, headache, evil qi, heat, *xiaoke*, arthralgia, eye problem; physical strengthen	Plant descriptions with illustration, identification by morphology	Su, 1994

1098	*证类本草* *Zhenglei Bencao*	Leaf, fruit, root	Treat rheumatism, headache, evil qi, heat, *xiaoke*, arthralgia; physical strengthen, anti-aging; leaf for tea and cooking as medicated food	Plant descriptions with illustration, identification by morphology; not to be used with cheese	Tang, 1982
1119	*本草衍义* *Bencao Yanyi*	Bark, fruit, root bark	NM	Plant description, and comments on the current use	Kou, 1990
Ca. 1238-1248	*汤液本草* *Tangye Bencao*	Root	Cited the former herbals, add meridian tropism	Only the root was mentioned	Wang, 1987
Ca. 1314-1320	*饮膳正要* *Yinshan Zhengyao*	Fruit, leaf	Extend longevity, anti-aging, anti-fatigue, enhance *yang* by medicated diets.	Fruit tea, goji wine, leaf lamb soup	Hu, 2009
1406	*救荒本草* *Jiuhuang Bencao*	Fruit, leaf	Fruit as food, leaf for tea	Include plant descriptions with illustration	Zhu, 2008
1505	*本草品汇精要* *Bencao Pinhui Jingyao*	Leaf, fruit, seedling	Treat evil qi, heat, *xiaoke*, and arthralgia; physical strengthen, anti-aging, antipyretic	Add incompatibility with other drugs	Liu, 1956
1565	*本草蒙筌* *Bencao Mengquan*	Seedling, fruit, root	Nourish *yin* and *yang*, protect eyesight, mind tranquilizing, calm blood, seedling as vegetable	Adulteration with honey, include identification of plant	Chen, 1988
1596	*本草纲目* *Bencao Gangmu*	Leaf, fruit, root, flower seedling,	Food and medicine, Summary of earlier herbals	Summary of earlier herbals, with Li's personal comments.	Li, 1954
1598	*药鉴* *Yaojian*	Fruit, root bark	Fruit sweet-bitter, nourish *yin* and *yang*, improve eyesight and hearing, mind tranquilizing, kidney; root bark bitter, calm blood, relief hectic fever	Root bark and fruit were recorded as 2 individual drugs separately	Du, 1975
1624	*本草汇言* *Bencao Huiyan*	Fruit, root bark	Fruit ascending or descending, root bark descending	Summary of former herbals, with formulas, lei include fruit processing	Ni, 2005
Ca. 1644-1911	*本草撮要* *Bencao Cuoyao*	Fruit, root bark	Fruit sweet and cold, nourish liver, root bark relief fever	With several compatibilities	Chen, 1985
1647	*本草乘雅半偈* *Bencao Chenya Banji*	Fruit, root bark	Treat evil qi, heat, *xiaoke*, and arthralgia; physical strengthen, anti-aging	With plant description, add the habit of growth and development	Lu, 1986
1691	*本草新编* *Bencao Xinbian*	Fruit, root bark	Fruit improves *yang*, while root bark improves *yin;* the dose of root bark was demonstrated	Sweet-bitter, TCM theory was added	Chen, 2008

1761	得配本草 *Depei Bencao*	Fruit, seedling and leaf, root bark	The compatibilities with other herbs, contraindications, was discussed; as medicine, tea, and medicated diet	Sweet, warm	Yan, 1958
1833	本草述钩元 *Bencao Shu Gouyuan*	Seedling, root, fruit	Antipyretic, nourish, anti-fatigue, treat sores; with formulas, and the theory were discussed; medicine, food, tea	Sweet, flat	Yang, 1958
1848	植物名实图考 *Zhiwu Mingshi Tukao*	Leaf, fruit, root	Tea, food, medicine use	Excerpt of herbals and dictionaries	Wu, 1959
1911	补图本草备要 *Butu Bencaobeiyao*	Fruit, root	With illustrations of plants, by which the plant could not be identified; summary of before	Sweet, flat, TCM theory	Jiang, 1911
1935	中国药学大辞典 *Zhongguo Yaoxue Dacidian*	Fruit, root bark	A summary of former herbals, introduced the concept of scientific name, however a wrong name was used	Summarize the earlier by time; Theory, recipes were included	Chen, 1935
1999	中华本草 *Zhonghua Bencao*	Fruit, root bark, leaf	Immuno-modulatory, anti-aging, anti-cancer, hepatoprotective, hematogenesis, hypoglycemic, treat sterilitas virilis; toxicity and contraindication was mentioned; prescriptions were included	The plants and the *materia medica* used were precisely described with illustration and microscopic characteristics; pharmacological evidences were included	*Zhonghua Bencao* Editorial Board, 1999
2002	新编中药志 *Xinbian Zhongyaozhi*	Fruit	Immuno-modulatory, anti-aging, anti-cancer, hepatoprotective; TLC was introduced for identification; identification key of the used species were included	The identification technology was improved	Xiao, 2002
2006	中药大辞典 *Zhongyao Da Cidian*	Fruit, root bark, leaf	Immuno-modulatory, anti-aging, anti-cancer, hepatoprotective, hematogenesis, hypoglycemic, antibacterial; with medicine formulas and medicated diet recipes; clinic reports were added	Description is clear and usages are practical	Nanjing TCM University, 2006

* Appendix to chapter 1. ** These references are to chapter.

S2 Questionnaires to different stakeholders in goji value chains

S2.1 Questionnaire (A) for farmers used in fieldwork

Occupation	Gender	Ethnicity	Age	Education level	Year of working

Goji acreage	Mu	Yield per Mu	Kg
In a cooperative	Y/N	Other crops acreage	Mu
Pesticides and fertilizer cost	Yuan/Mu	Amount spent on land	Yuan/Mu
Drying cost	Yuan/Mu	Pest Control and Prevention	Personal/Unity measures
Certified grade of quality	Pollution-free/Green/Organical	Products	Dried/fresh fruits
Family size		Number of full labor	
Monthly living cost	Yuan	People working on goji	

A1. What makes good quality? What do you think is the most important technology for getting a high yield and good quality?
A2. About Family members: students? The old? Other people's job? Total income and cost?
A3. Where are the cultivating technologies from? What species do you plant? Where do you get the seedlings from?
A4. Pesticides and fertilizer application: Types, quantities, frequency, benefit. Do you know safety use of them?
A5. What is the most efficient method for drying according to your experience? What method do you use?
A6. Please describe what goji materials can get a high price? Whom do you sell goji to? If the price is not acceptable, what will you do?
A7. Do you know the price of other goji products? As well as the price of goji in other province? How? Can you use (do you have) smart phone or computer to visit the web?
A8. Why do you want to start/stop cultivating goji?(For the new/past goji farmer only)
A9. Are you satisfied with the present production model and why? What would you like to change to improve the situation?

S2.2 Questionnaire (B) for pickers used in fieldwork

Occupation	Gender	Ethnicity	Age	Education level	Year of working

Other occupations		Hometown	
Organized pickers	Y/N	Salary for picking	Yuan/kg
Workdays	Day	Daily cost during workdays	Yuan
Work hours per day	Hour	Daily harvest volume	kg
Family size		Number of full labor	
Monthly living cost	Yuan	Number of people work on goji	

What makes good quality? What do you think is the most important technology for getting a high yield and good quality?
About Family members: students? The old? Other people's job? Total income and cost?
Are there any technical essentials for picking? Does picking affect the quality of goji?
Who decide the price for picking? And what are the impact factors of price?
What do you think of the working conditions here?
How do the farmers pay you? Brokerage of organizer?
Do you care about the price of goji products? How can you get the goji information?
How many people from your family come here for the picking? Is your family supporting you to work here?
Can you conjecture the income of farmers?
Why do you want to join in picking goji?
More to say:

S2.3 Questionnaire (c) for middlemen used in fieldwork

Occupation	Gender	Ethnicity	Age	Education level	Year of working

Supply of goji		Stock of goji	Kg
Store form	Online/Chain/XB	Certified grade of quality	Pollution-free/Green/Organical
Number of product type		Number of staff	
Cost of the shop		Salary of staff	Yuan/month
Transportation cost		Packing cost	
Monthly turnover		Monthly payoff	
Family size		Number of full labor	
Monthly living cost	Yuan	People working on goji	

What do you think is the most important technology for getting a high yield and good quality?
About Family members: students? The old? Other people's job? Total income and cost?
Please describe the features of good quality goji? Do the good goji have a high price?
What do the consumers most care about goji?
How do you know the price of goji products? As well as the price of goji in other province? Can you use (do you have) smart phone or computer to visit the web?
Do you have any suggestion to improve the quality of goji products?
What kind of goji store will be the most popular in the future?
To what extend will your income be affected by the fluctuations in goji price?
Are you satisfied with the present production model and why? Do you want to change something to improve the situation?

S2.4 Questionnaire (D) for retailers used in fieldwork

Occupation	Gender	Ethnicity	Age	Education level	Year of working

Supply of goji		Stock of goji	Kg
Store form	Online/Chain/XB	Certified grade of quality	Pollution-free/Green/Organical
Number of product type		Number of staff	
Cost of the shop		Salary of staff	Yuan/month
Transportation cost		Packing cost	
Monthly turnover		Monthly payoff	
Family size		Number of full labor	
Monthly living cost	Yuan	People working on goji	

What do you think is the most important technology for getting a high yield and good quality?
About Family members: students? The old? Other people’s job? Total income and cost?
Please describe the features of good quality goji? Do the good goji have a high price?
What do the consumers most care about goji?
How do you know the price of goji products? As well as the price of goji in other province? Can you use (do you have) smart phone or computer to visit the web?
Do you have any suggestion to improve the quality of goji products?
What kind of goji store will be the most popular in the future?
To what extend will your income be affected by the fluctuations in goji price?
Are you satisfied with the present production model and why? Do you want to change something to improve the situation?

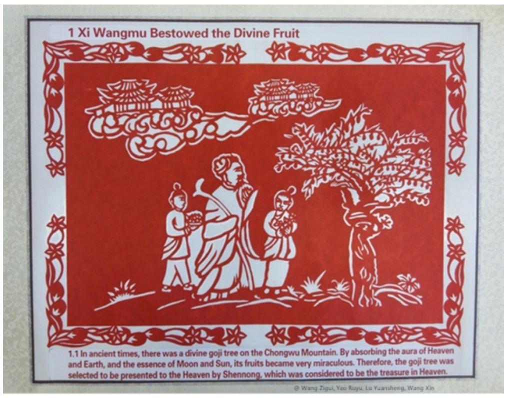
S2.5 Questionnaire (E) for companies used in fieldwork

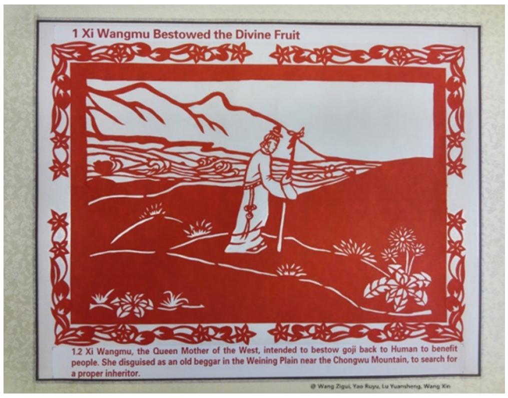
Firm size and qualification:
Scope of business: cultivation   fresh fruit   dried fruit   deeper-processed products
What do you do for quality control? Species, pesticides, fertilizer, drying, buying…
Do you have export business? Is it stricter than the domestic trading? Which sides?
Do you have any plan for new business and why?
Please evaluate the present production model:

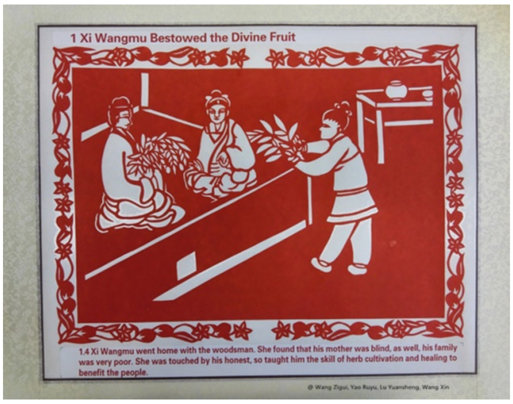
S2.6 Questionnaire (F) for village leaders used in fieldwork

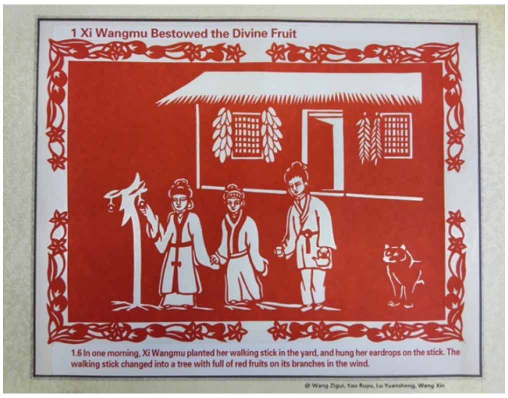
Village size:			
Population		Ethnicity	
People engaged in goji		Total farmland	
People in cultivation		Farmland for goji	
People in processing		Cultivation history	
People in marketing		Monthly living cost per person	
How many kind of production models are there in the village?			
Are there any farmers start/ stop cultivating goji? Why?			
Are there any non-government organizations for goji production? And what can they do for the farmers?			
What do they do for quality control? Species, pesticides, fertilizer, drying, buying…			
What makes good quality? What do you think is the most important technology for getting a high yield and good quality?			
Please evaluate the present production model. Do you want to change something to improve?			

S3 Photos of goji legends papercuts published at: http://www.ethnopharmacology.org/index.htm









S4 Photos during fieldwork


Harvesting, 2015


Collecting fresh goji, 2015


Drying goji in open air, 2015


Drying by artificial drying room, 2015


Middleman and farmer in Qinghai, 2015


Wholesale in distribution centre, 2015


Retailer, 2015


A pot of goji tea, 2015


A giant goji tree, 2016


Making papercuts, 2016


White goji and black goji, 2015


Interviewing an experienced goji farmer, 2015


At national Lycium germplasm resource garden, 201


Sampling in Hebei, 2016


Xinjiang goji market, 2015


Author at Zhongguo Gouqi Guan, 2014

CURRICULUM VITAE

BASIC INFORMATION:

Family Name: YAO
First Name: Ruyu
Date of Birth: 11 March, 1988
Nationality: Chinese

EDUCATION:

2014-present* Ph.D. student, major in Ethnobotany, at Institute of Systematic and Evolutionary Botany, University of Zurich, Switzerland. Advisor: Prof. Dr. Peter Linder; Supervised by Dr. Caroline Weckerle and Prof. Dr. Michael Heinrich (UCL School of Pharmacy). * Defensed on 14th May, 2018.

2010-2013 Master's Degree in Agronomy , major in Pharmaceutical Botany, at Sichuan Agricultural University, PR China. Supervised by Prof. Dr. Xingfu Chen.
Tittle of thesis: Studies on Harvesting and Storage Characteristics of *Bupleurum chinense* Seeds from Qingchuan County

2006-2010 Bachelor's Degree in Agronomy, major in Cultivation and Authentication of Chinese Herbal Medicine, at Sichuan Agricultural University, PR China.

2003-2006 High School student, at Luojiang Middle School of Sichuan Province, PR China.

RESEARCH INTERESTS:

Food and medicinal use of plants, culture and traditional usage of plants, quality control and value chain analysis of plant-derived products

PUBLICATIONS:

Yao, R., Heinrich, M., Zou Y., Reich, E., Zhang, X., Chen, Y., and Weckerle, C. (2018) Quality variation of goji (fruits of *Lycium* spp.) in China: A comparative morphological and metabolomic analysis. Frontiers in Pharmacology 9, 151.

Yao, R., Heinrich, M., and Weckerle, C.S. (2018). The genus *Lycium* as food and medicine: A botanical, ethnobotanical and historical review. Journal of Ethnopharmacology 212, 50-66.

Yao, R., Huang, C., Chen, X., Yin, Z., Fu, Y., Li, L., Feng, B.,et al. (2018). Two complement fixing pectic polysaccharides from pedicel of *Lycium barbarum* L. promote cellular antioxidant defense. International Journal of Biological Macromolecules 112, 356-363.

Nenadic, M., Rüegg, J., **Yao, R.** (2017). "How to achieve the transition of European agriculture towards self-sufficiency in protein supply," in Agriculture in Transformation : Concepts for agriculture production systems that are socially fair environmentally safe., ed. M. Paschke. (München: Idea Verlag), 114-116.

Yao, R., Heinrich, M., Wang, Z., Reich, E., Weckerle, C. Quality control of goji (fruit of *Lycium barbarum* L.): A value chain analysis perspective. (submitted)

CONFERENCES:

Ruyu Yao, Michael Heinrich, Eike Reich, Anthony Booker, Caroline Weckerle, 2017. How does the quality change among goji berry (fruits of *Lycium* spp.) of different regions in China? A quality assessment based on HPTLC fingerprint and ^{1}H NMR metabolomics analysis. Phytopharm 2017, Graz, Austria. Poster.

Ruyu Yao, 2017. *Lycium* spp. : A cross-cultural study of its use as medicine and food. MedPlant (www.MedPlant.eu) Initial Training Network (ITN) Conference 2017, Bern, Switzerland. Oral presentation.

Ruyu Yao, 2016. *Lycium* spp. : A cross-cultural study of its use as medicine and food. Food and Medical Traditions from the Plant World: Exploring Herbal Uses, London, UK. Poster.

Ruyu Yao, 2016. Simultaneous analysis of flavonoids, betaine, and monosaccharides in goji (fruits of *Lycium* spp.) using HPTLC with SPE. The 16th Congress of International Society of Ethnopharmacology, Yulin, China. Oral presentation.

Ruyu Yao, Gary Stafford, Michael Heinrich, Anita Ankli, Caroline Weckerle, 2015. Rapid identification of goji berry (fruit of *Lycium* spp.) from different provinces in China by HPTLC and sensory properties analysis. The 15th Congress of International Society of Ethnopharmacology, Petra, Jordan. Poster.

OUTREACH ACTIVITIES:

Public introduction for Springfestival of UZH Botanical Garden in 2014, and garden tours;
Public talk: "Goji (*Lycium* spp.), die Wunderbeere aus China", and goji exhibition;
Final reviewer of goji monograph by American Herbal Pharmacopoeia.

SCHOOLARSHIPS:

Chinese Government Schoolarship, No. 201306910001
Claraz Schenkung in year of 2015, 2016, and 2017

VISITING STUDYS:

2016.10-11	^{1}H NMR-based plant metabolomic analysis, supervised by Prof. Dr. Michael Heinrich, at UCL School of Pharmacy, UK
2015-2017	HPTLC-based herbal medicine identification, supervised by Dr. Eike Reich, for three months, at CAMAG Laboratory, Switzerland
2013.11-2014.1	DNA sequencing-based plant systematic analysis, supervised by Prof. Dr. Zhiduan Chen, at Institute of Botany, Chinese Academy of Sciences, China
2010.1-2	Cultivation management of herbal medicine, supervised by Dr. Zhendong Liu, at Sichuan Neautus TCM Co., Ltd., China

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